Sweet taste: GRNs, CNS and behaviors

Reporter: JSH SMS MMZ

Date: 2021/12/30

Environmental stimulus

Behavioral responses

nutritive substances: suagrs, amino acids, low salt

harmful substances: high salt, acids, bitter compounds

non-canonical modalities：fatty acids, carbonated water, polyamines, H2O2, bacterial lipopolysaccharide (LPS), ammonia, calcium …

receptors: Grs, Irs, Trp, and ppk receptors

powerful genetic model

“Sweet”

1.How various chemical cues are detected? ——JSH

2. How taste neurons connect to different higher-order neuronal circuits? ——SMS

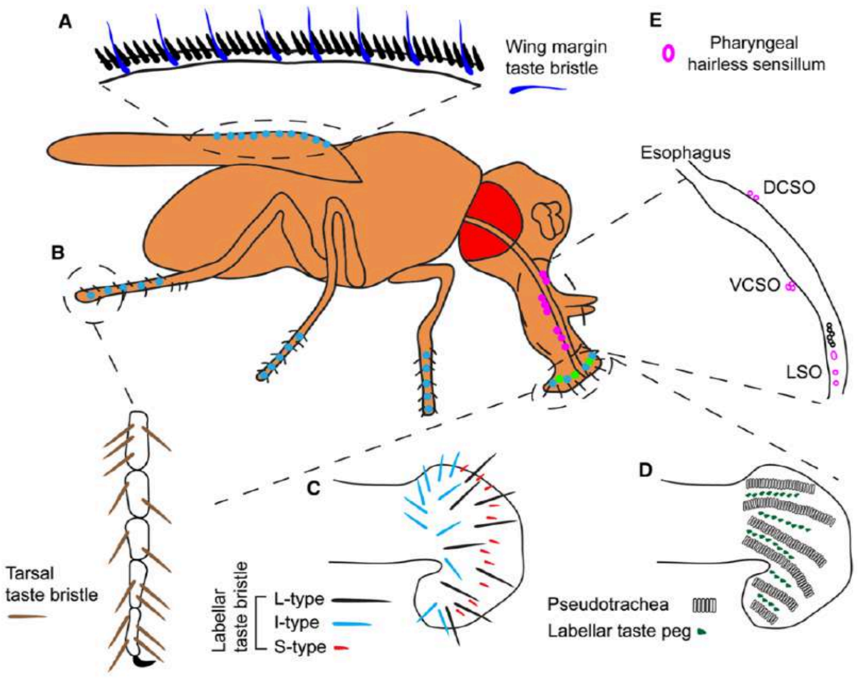
3. How input from GRNs is evaluated for complex taste-associated behaviors? ——MMZ

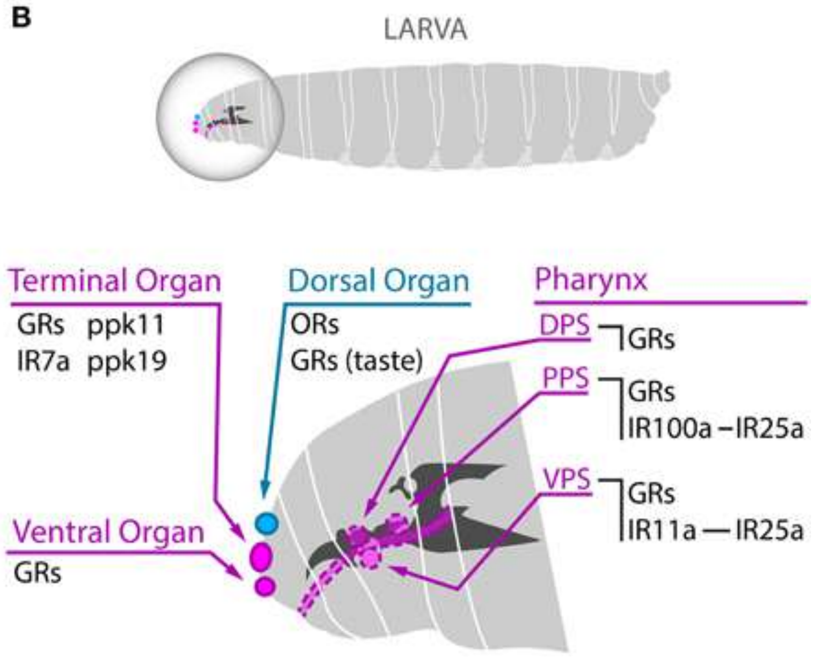
ONE.

Taste Detection By Sensory Neurons

JSH

The distribution of taste organs in adult *Drosophila* and larval





External taste organs: 1.The anterior wing margins
2.Distal segments of the legs
3.The labellum

Internal taste organs: Three pharyngeal taste organs
labral sense organ (LSO), ventral cibarial sense organ (VCSO), dorsal cibarial sense organ (DCSO)

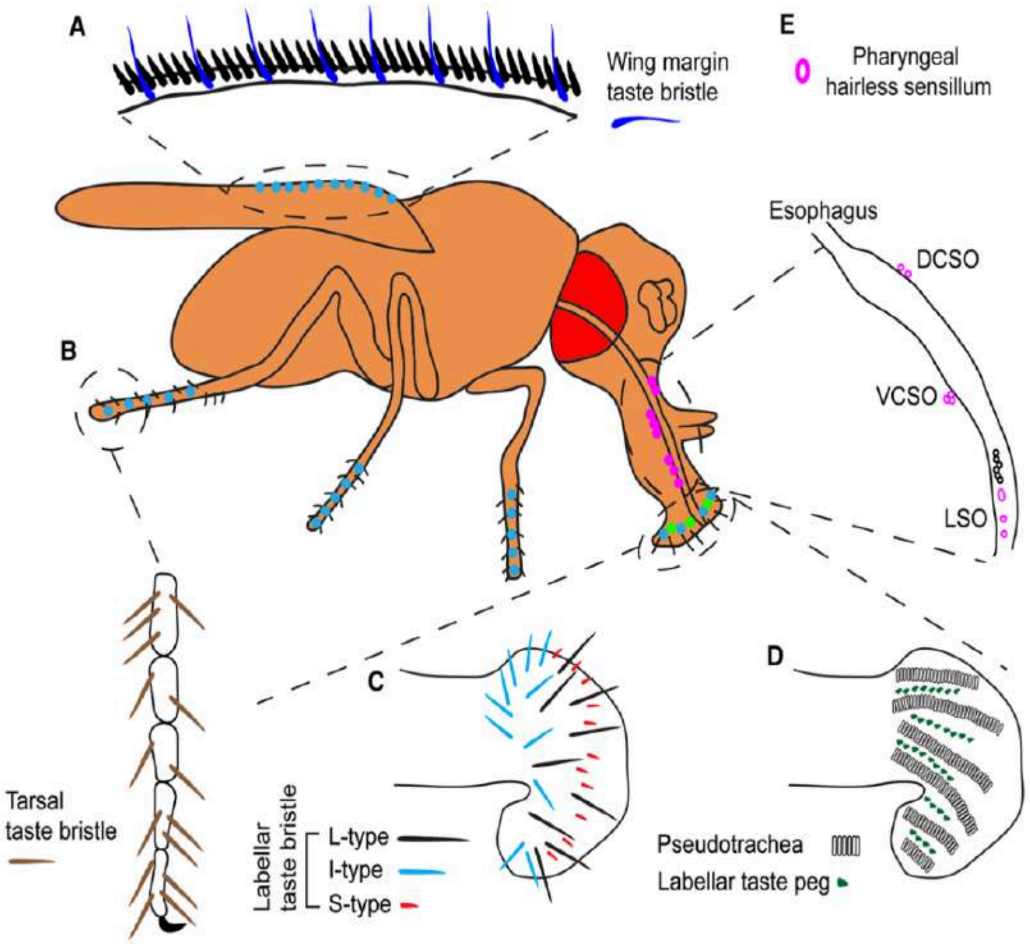
The larval taste system is simpler than that of the adult.

- ✓ The dorsal organ
- ✓ The terminal organ
- ✓ The ventral organ
- ✓ Three pharyngeal organs

Chen Y, Dahanukar A. Cellular and Molecular Life Sciences, 2020.

Ana DC, Diego G, Yael G. Frontiers in Ecology and Evolution, 2015.

Taste sensilla is the basic functional units of taste detection



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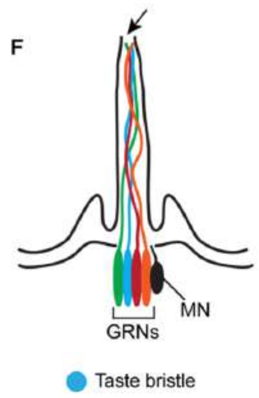
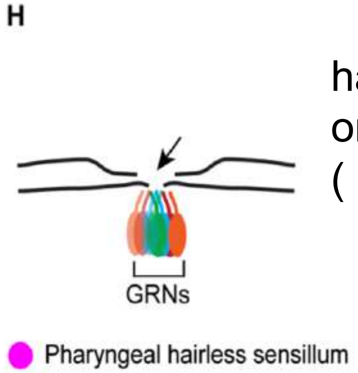


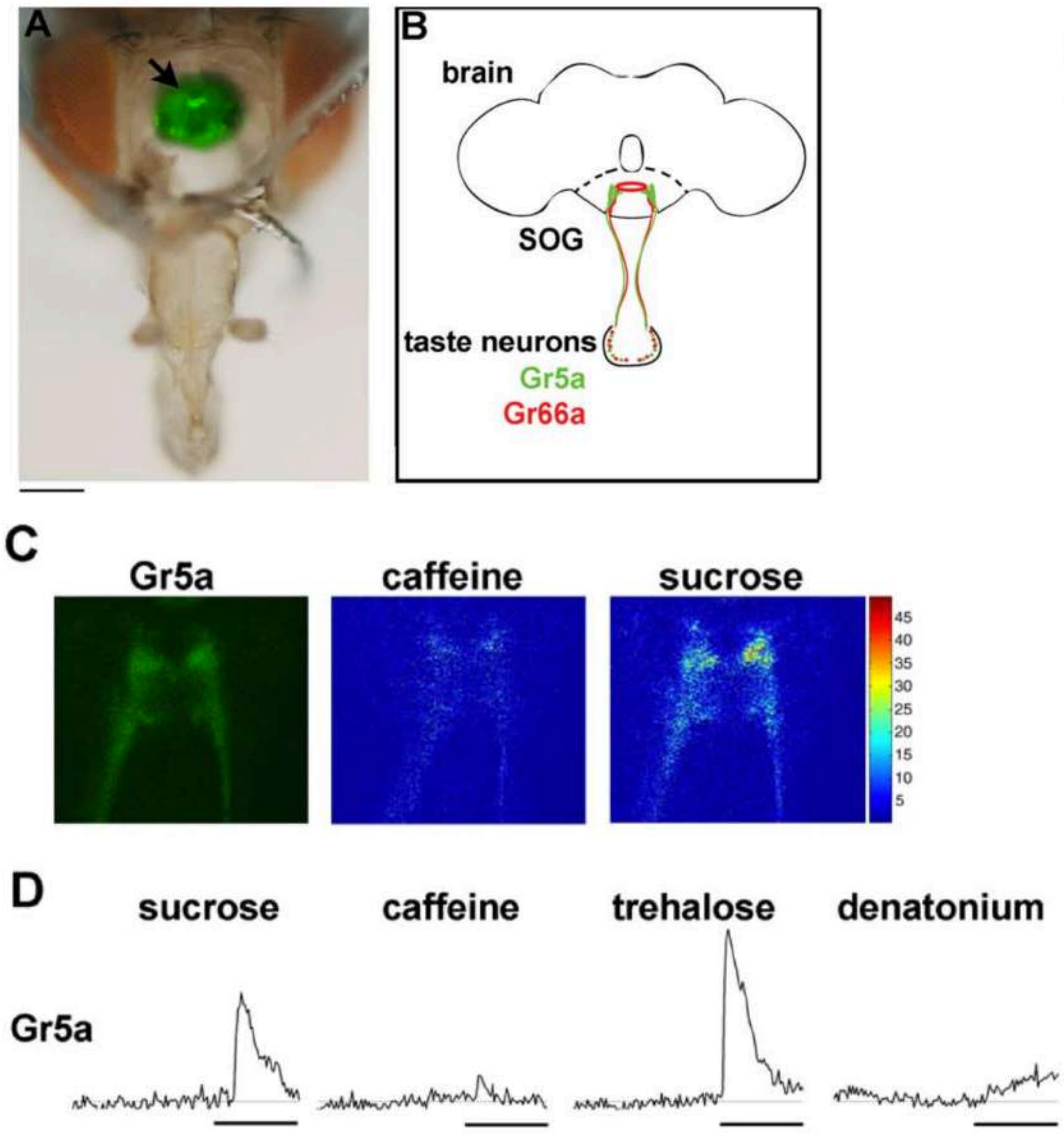
Labellum:~ 30 hairs on each half of the labellum
L (long), I (intermediate), and S (short)-type
a single mechanosensory neuron + 2~4 chemosensory neurons

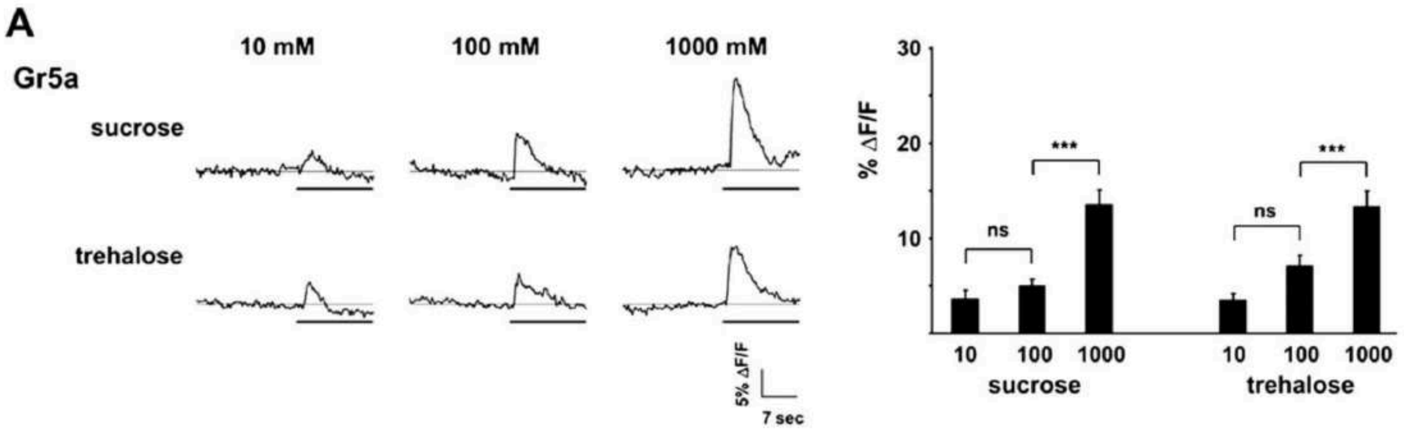
sexually dimorphic
one mechanosensory neuron + one chemosensory neuron

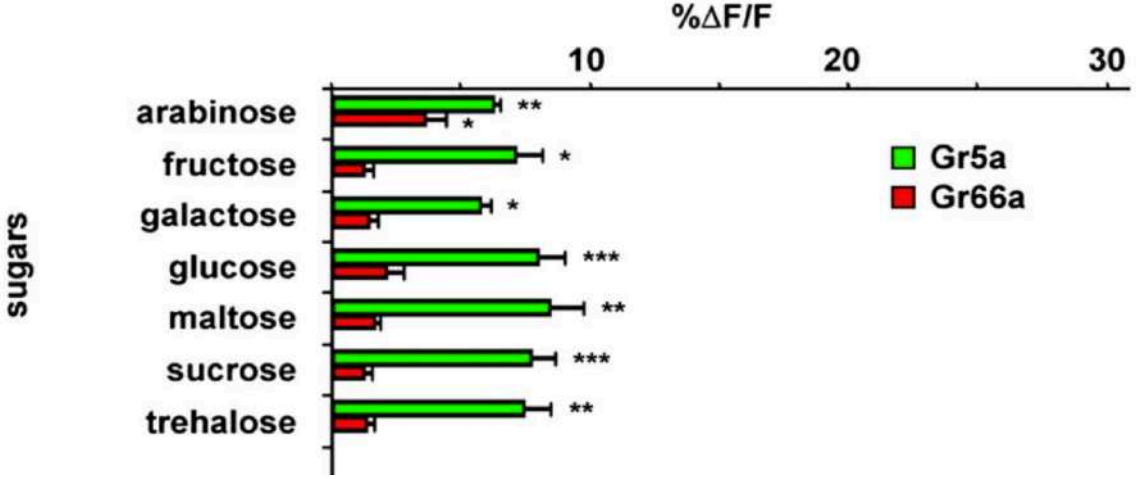


hairless
one to eight chemosensory neurons
(mechanosensory neurons)

Gr5a cells selectively respond to sugars

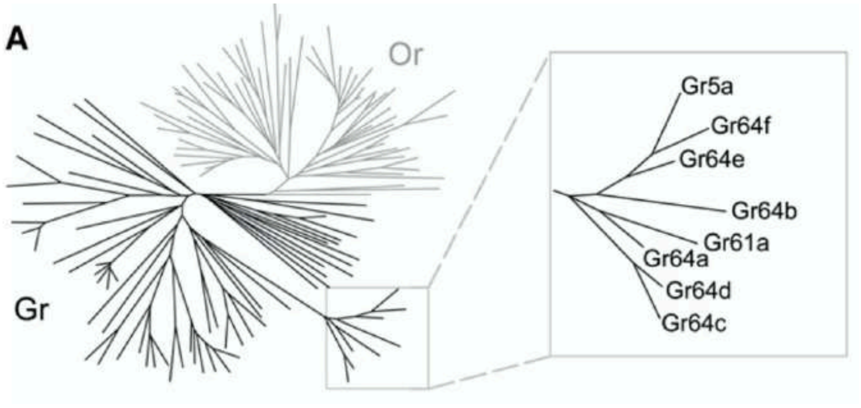


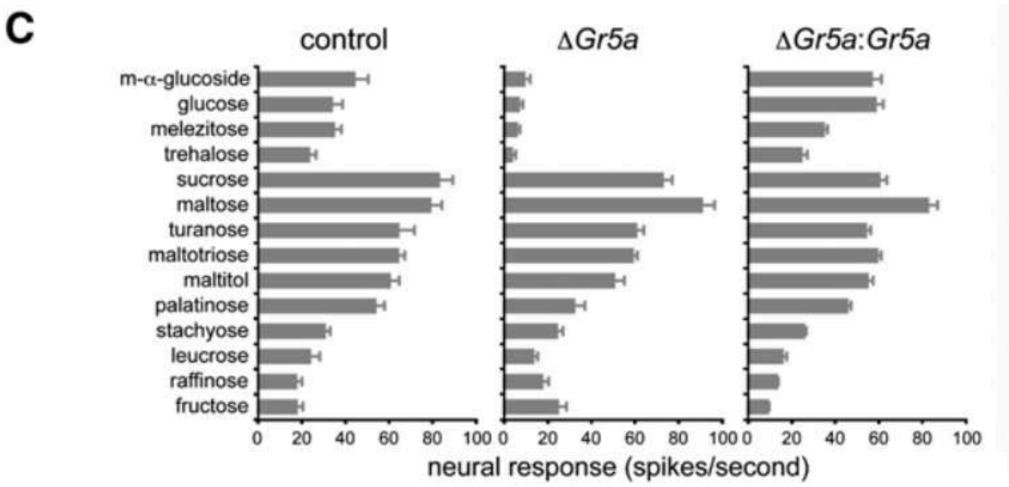


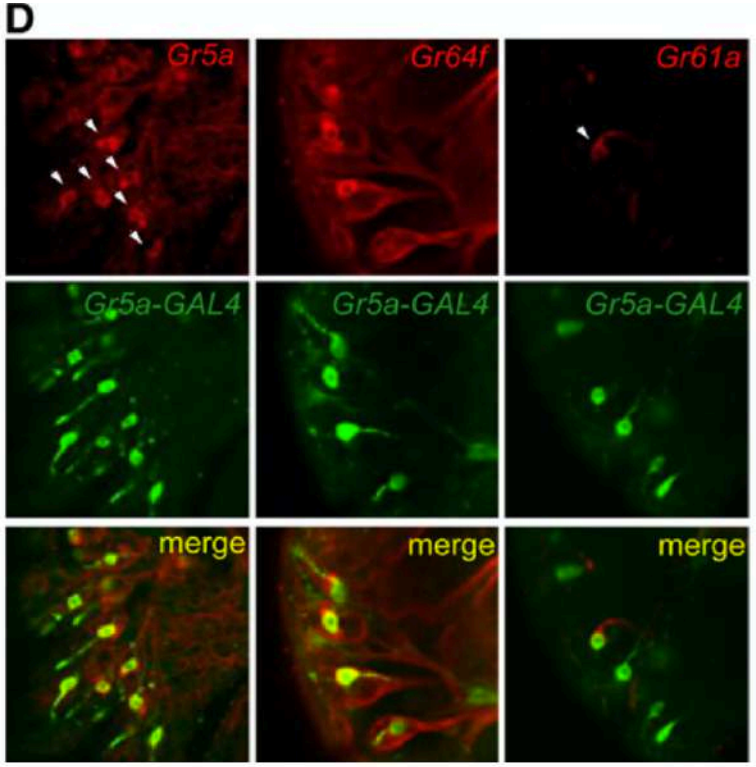


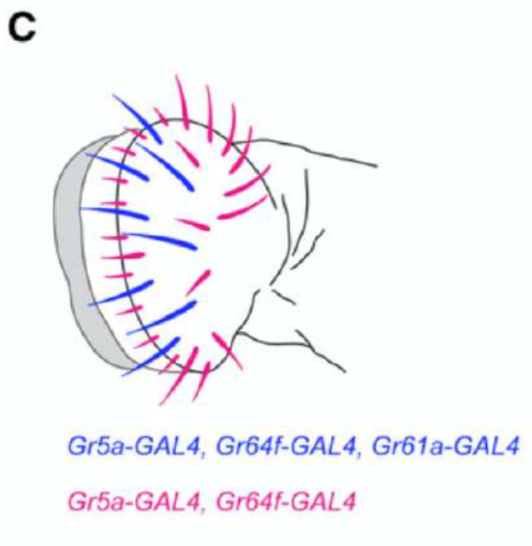
Marella S, Fischler W, Kong P, et al. Neuron, 2006.

Sugars are dependent on Gr5a or Gr64a for neuronal and behavioral responses



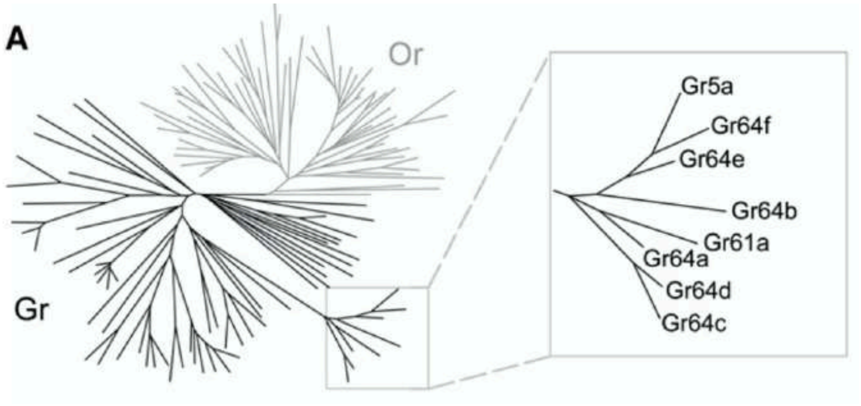


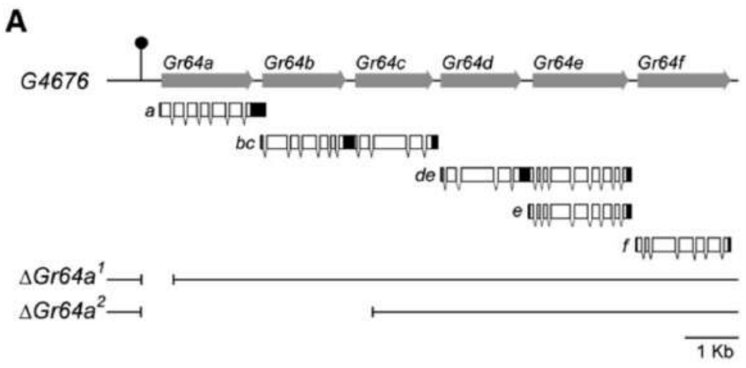


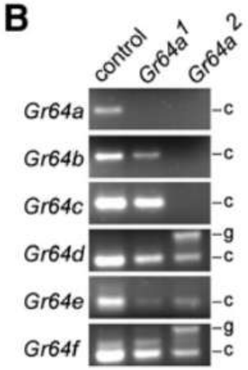


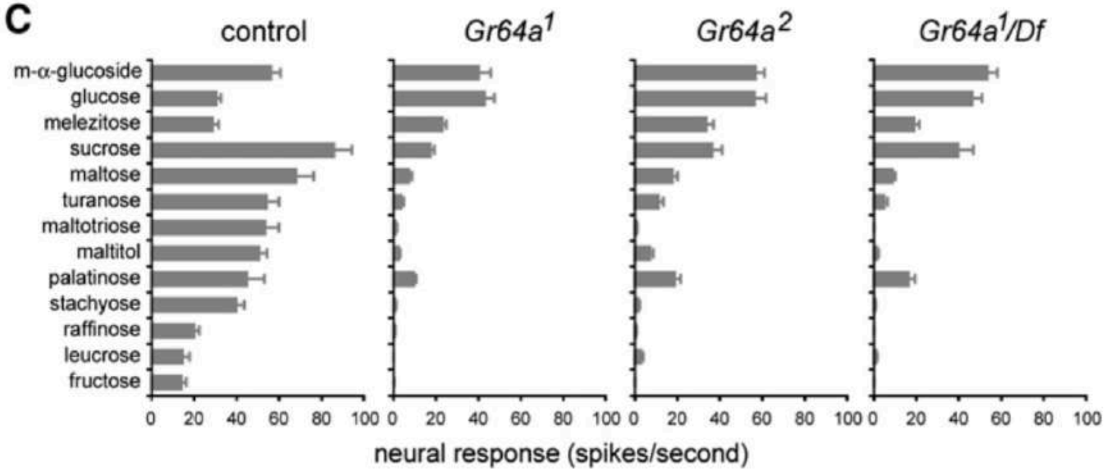
Dahanukar A , Lei Y T , Kwon J Y , et al. Neuron, 2007,

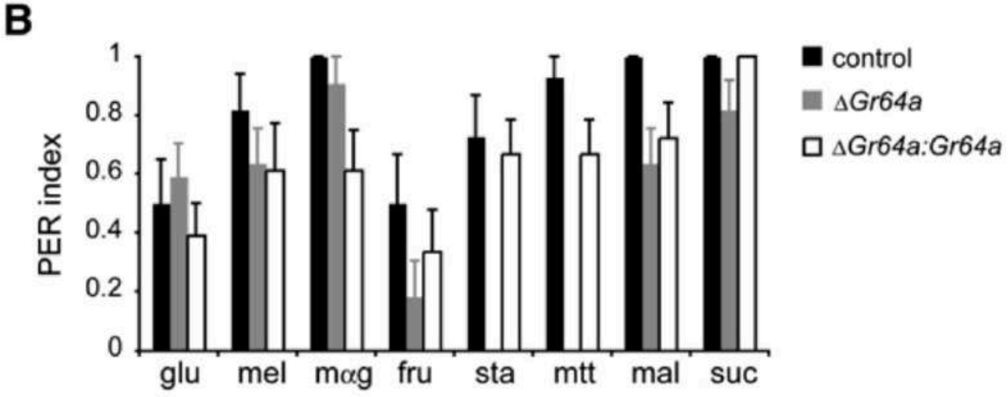
Sugars are dependent on Gr5a or Gr64a for neuronal and behavioral responses











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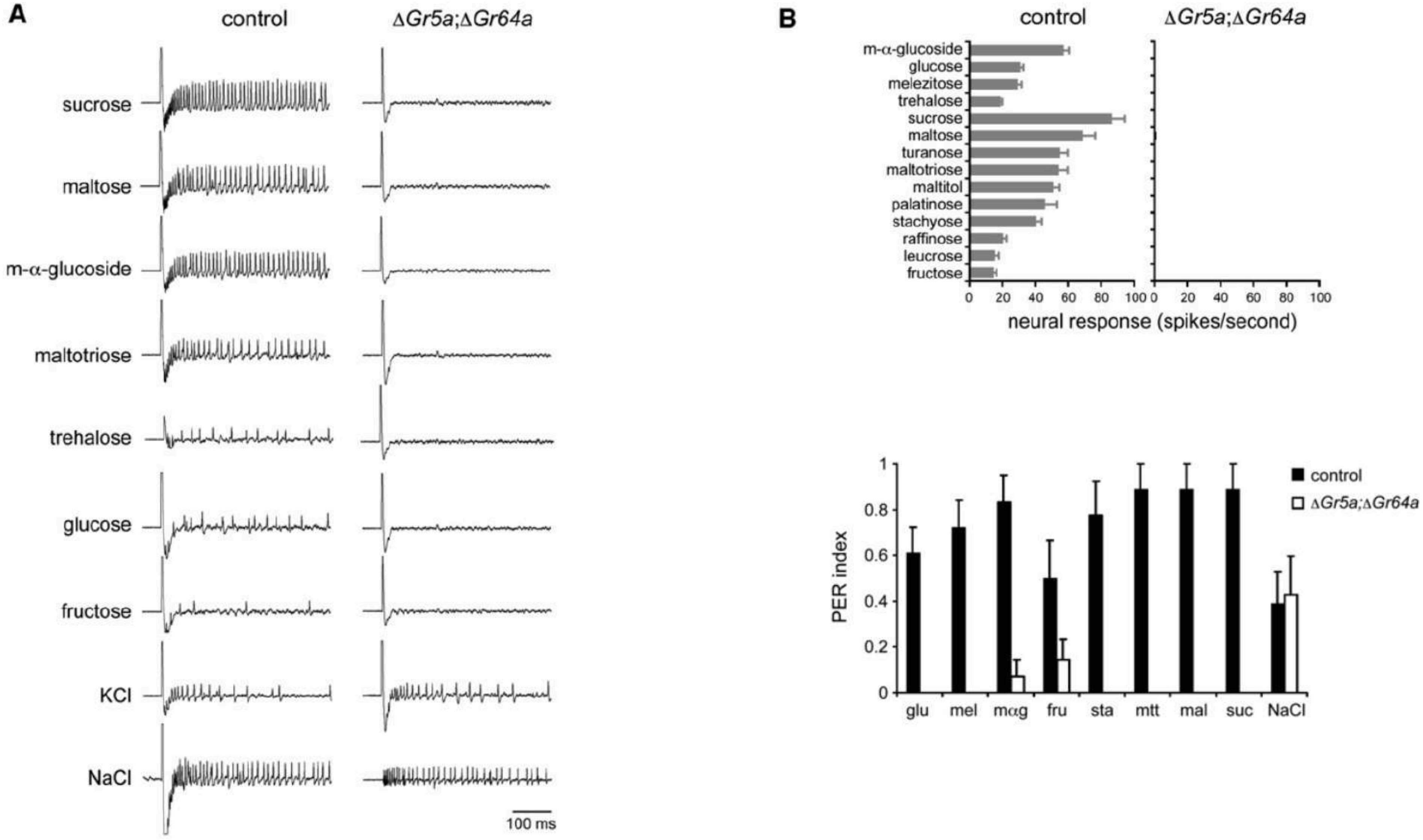
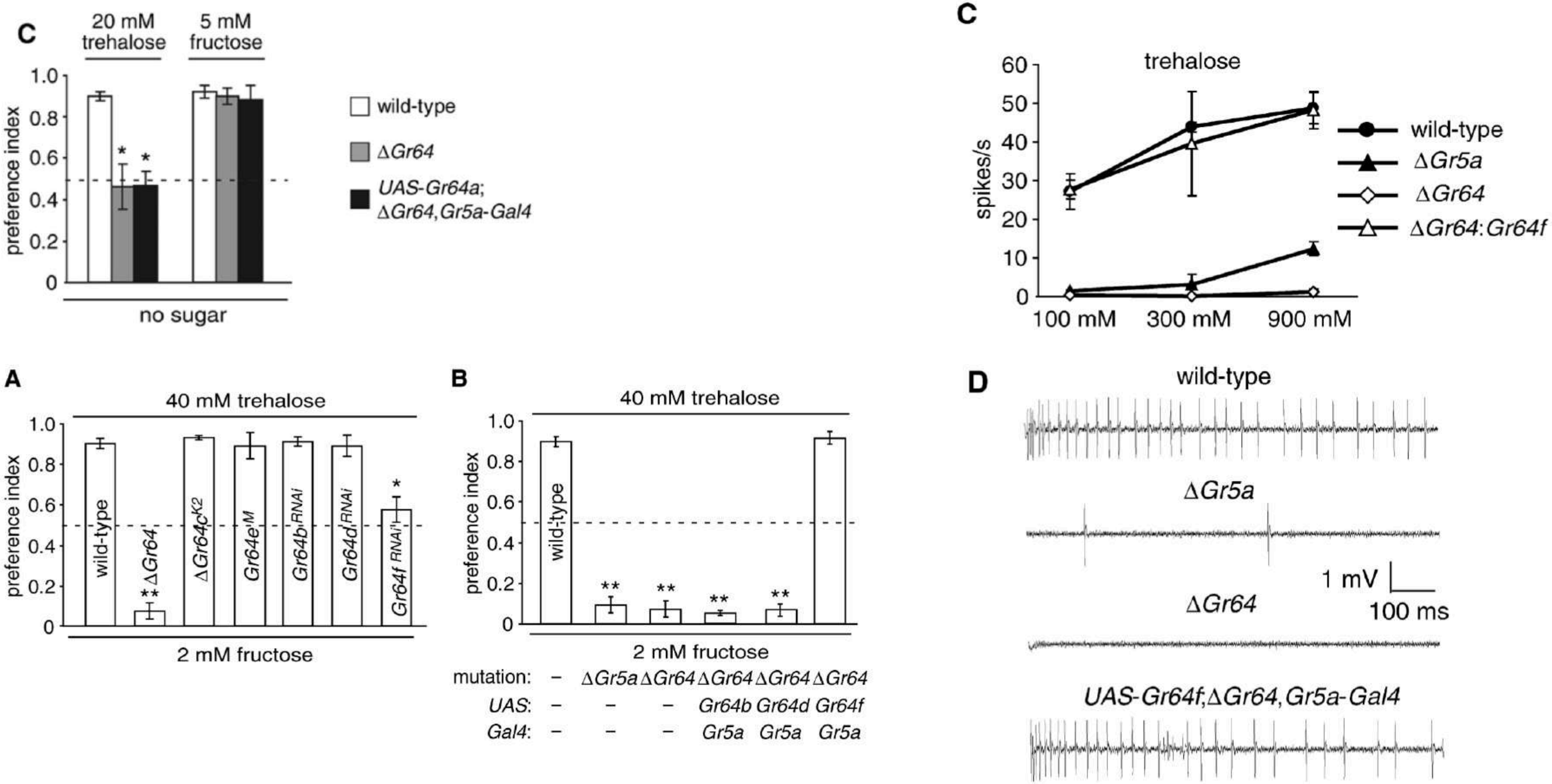


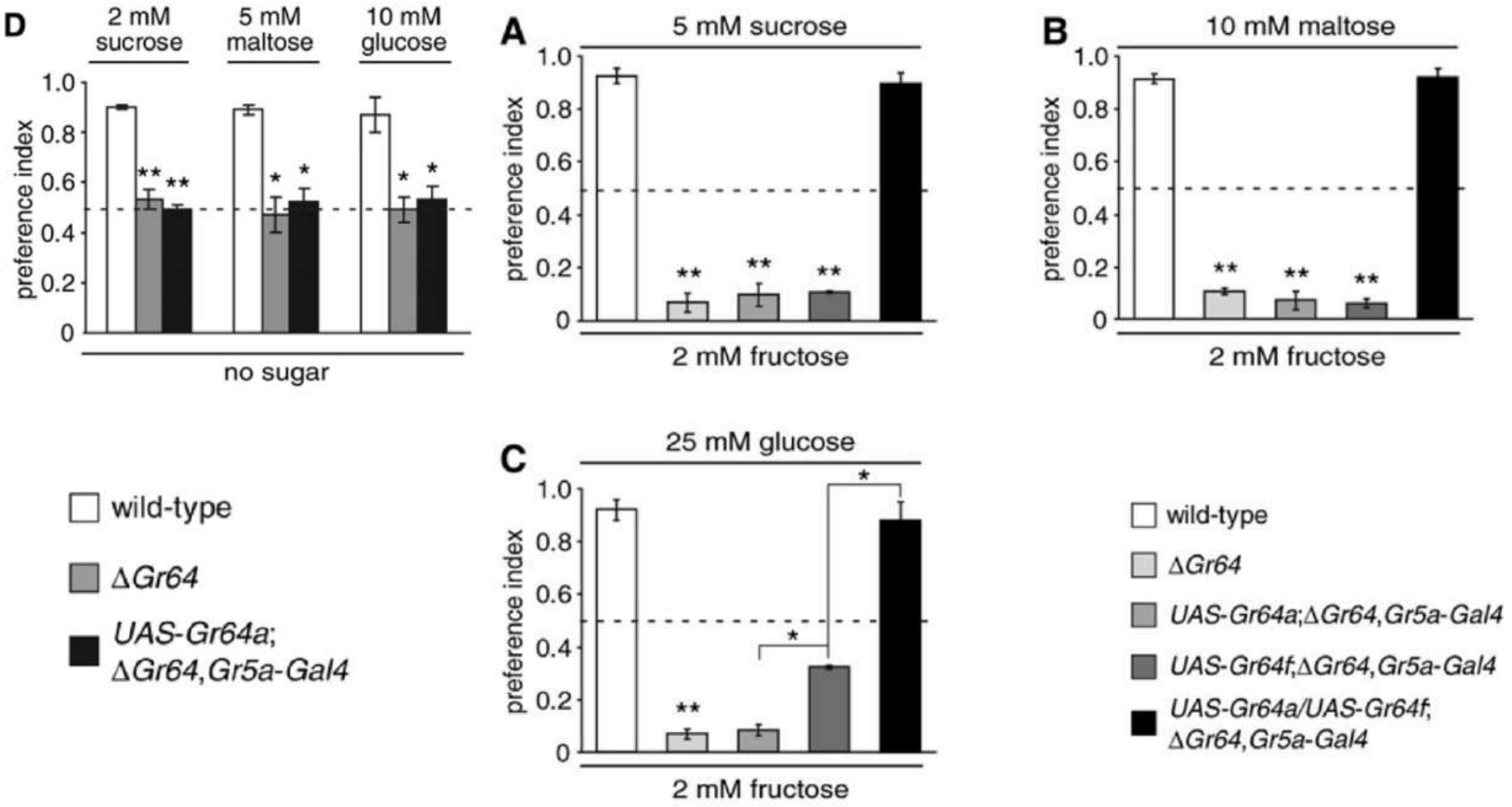
Dahanukar A , Lei Y T , Kwon J Y , et al. Neuron, 2007,

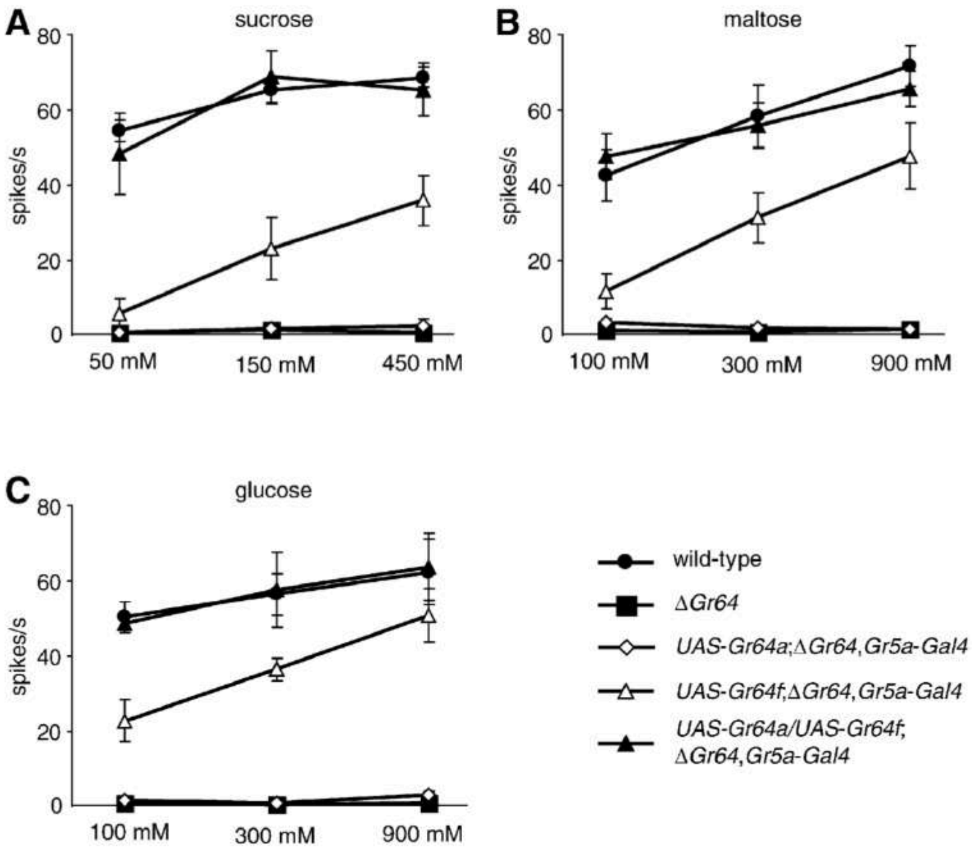
Gr64f is required to sense trehalose together with Gr5a



Jiao Y, Moon SJ, Wang X, et al.Current Biology.2008.

Gr64f is required in combination with Gr64a to detect sucrose, maltose, and glucose

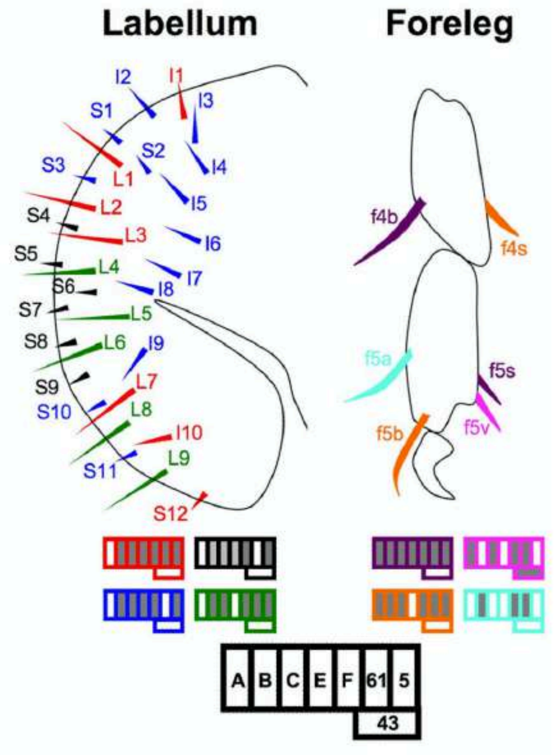




Jiao Y, Moon SJ, Wang X, et al.Current Biology.2008.

Sugar *Gr* genes are expressed in a combinatorial manner

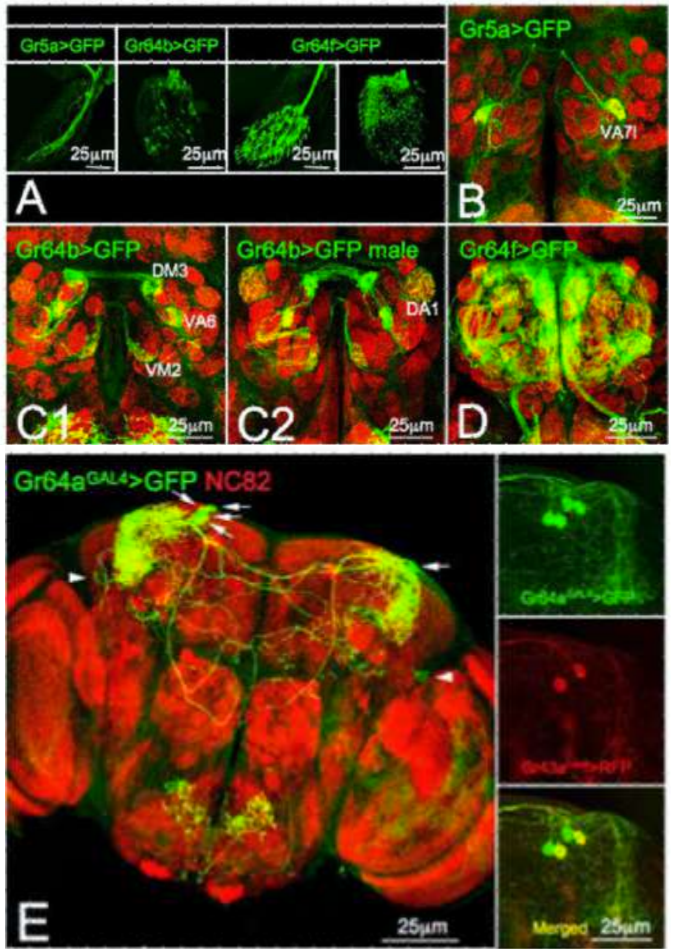
1.*Gr64a* is not expressed in labellar taste neurons



1. Each sugar *Gr* gene contributes to the detection of at least one sugar
2. PER response to every sugar, except melezitose, is affected by more than one sugar *Gr* mutation

Mut\sugar		Suc	Mal	Fru	Mel	Glu	Ara	Tre	Gly
Wild type	leg	8	8	8	8	8	8	8	8
	lab	8	8	8	8	8	8	8	8
Gr64a^{GAL4}	leg	8	5	5	8	8	6	8	3[1)]
	lab	8	8	8	8	8	7	8	3[1)]
Gr64b^{LEXA}	leg	8	6	8	8	7	7	7	2
	lab	8	8	8	8	8	7	8	2
Gr64c^{LEXA}	leg	5	4	6	8	7	5	8	3
	lab	8	7	7	8	8	5	8	7
Gr64e^{LEXA}	leg	7	8	8	8	8	6	8	2
	lab	8	8	7	8	8	6	8	4
Gr64f^{LEXA}	leg	7	6	7	6	3	5	5	7
	lab	8	8	6	8	6	6	8	8
Gr5a^{LEXA}	leg	8	4	8	8	5	6	4	5
	lab	5	4	4	5	7	7	5	7

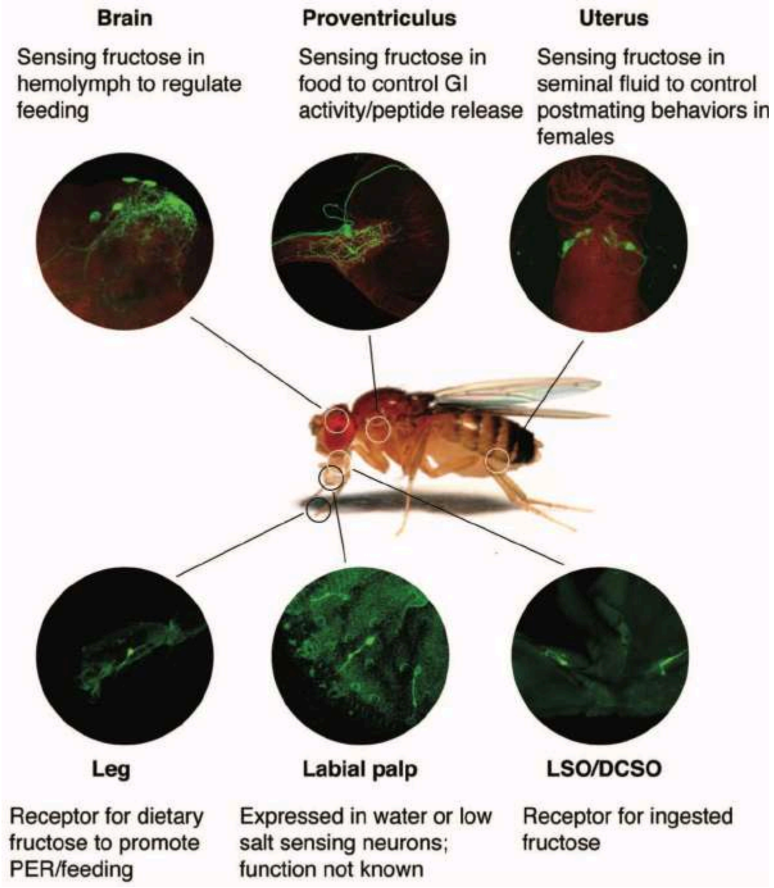
olfactory organs and brain

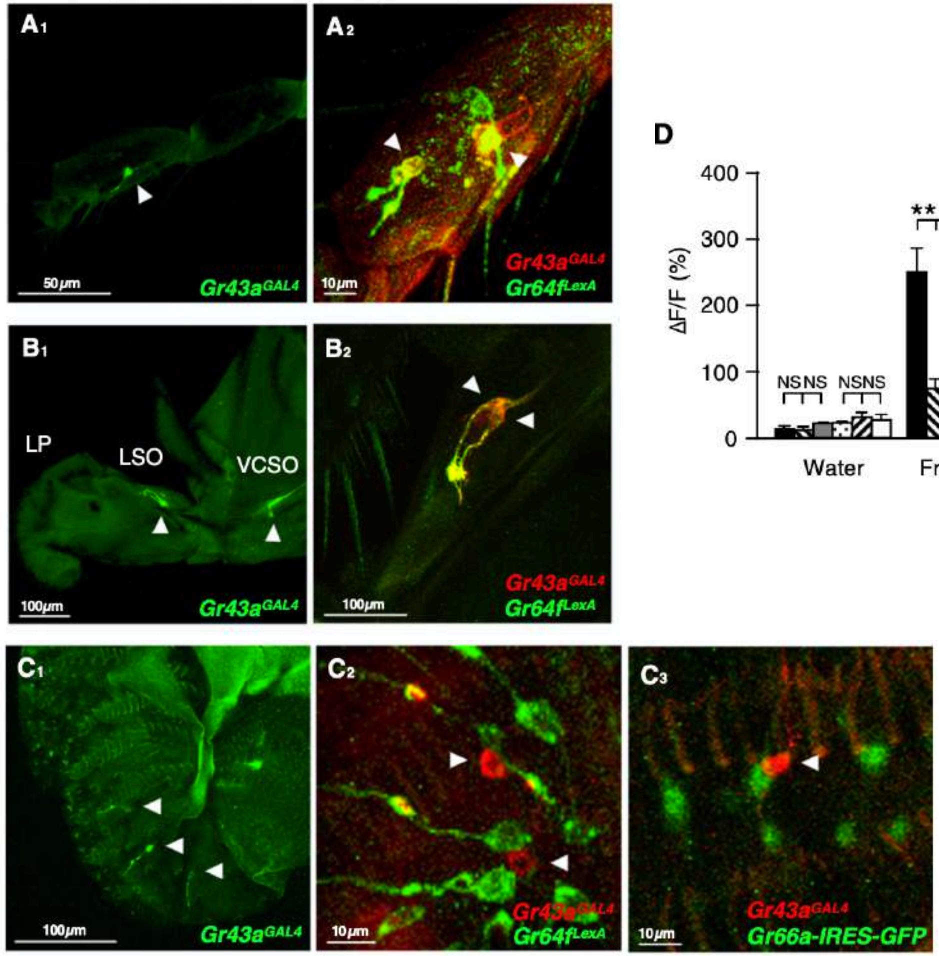


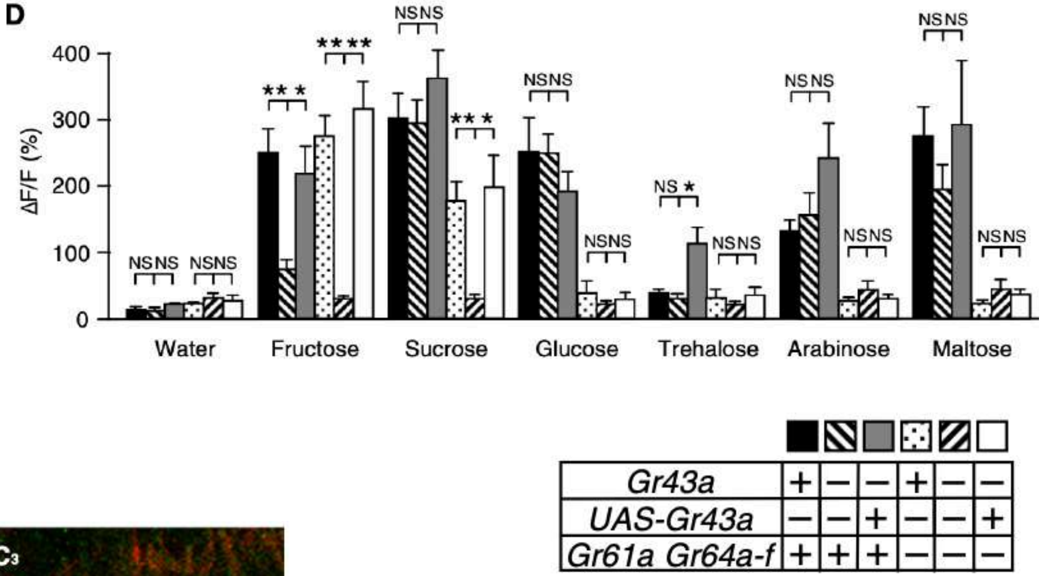
Fujii S , Yavuz A , Slone J, et al. Current Biology, 2015.

Gr43a functions as a narrowly tuned fructose receptor in taste neurons

an internal nutrient sensor





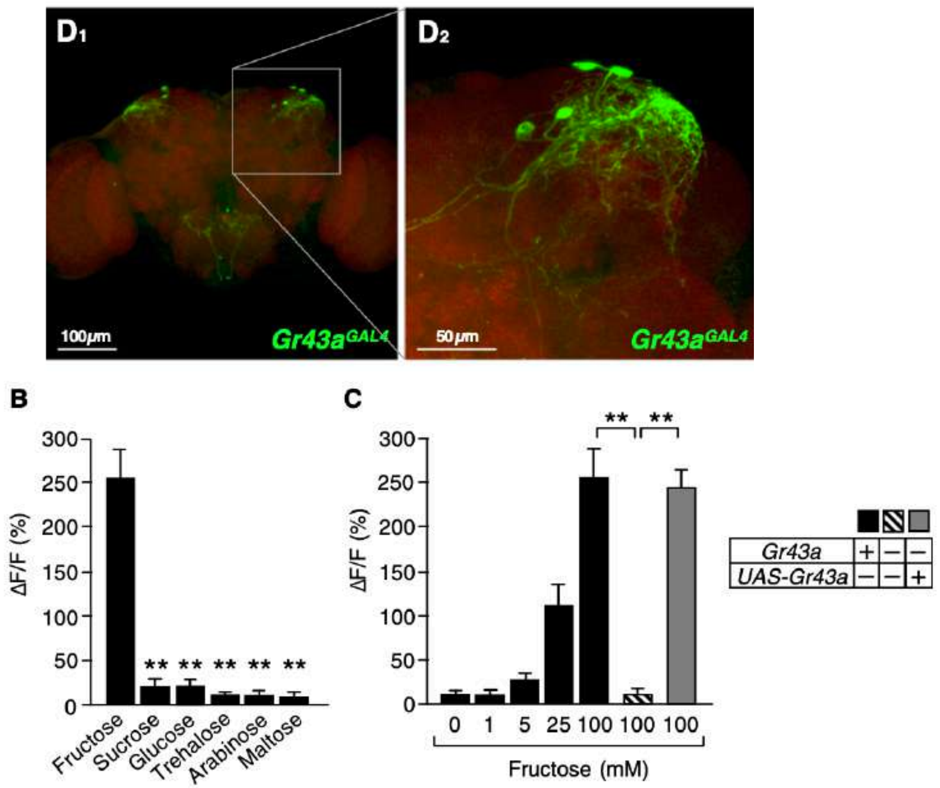


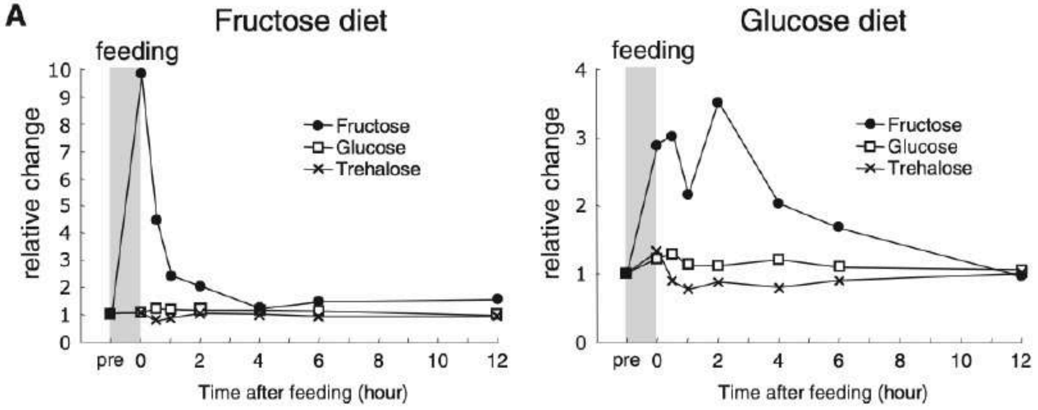
a taste receptor

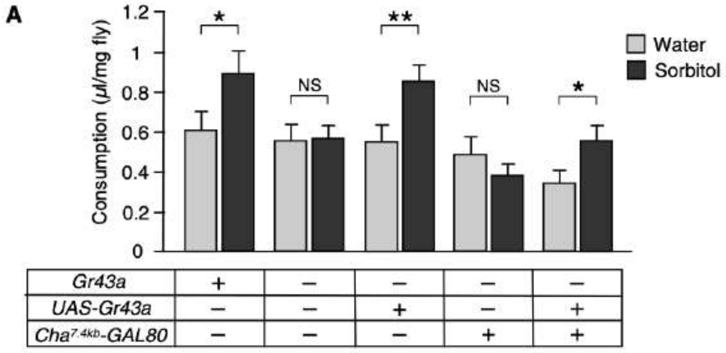
Miyamoto T, Amrein H. Fly, 2014.

Miyamoto T, Slone J , Song X , et al. Cell, 2012.

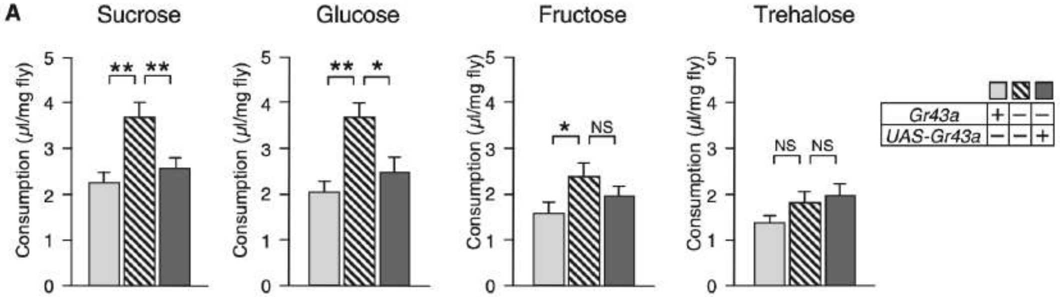
Gr43a functions as an internal nutrient sensor in the brain



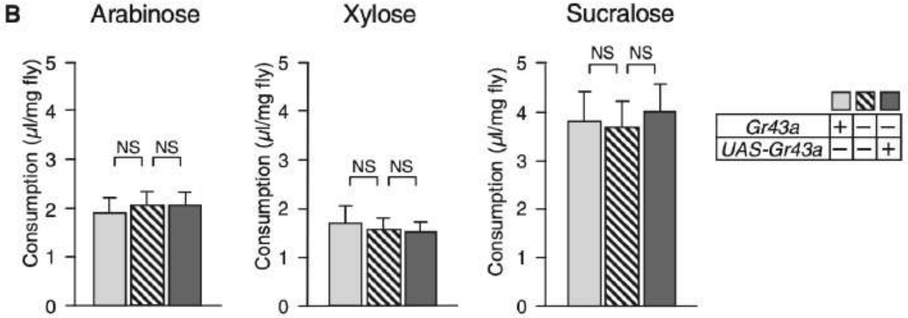




Sweet and nutritious

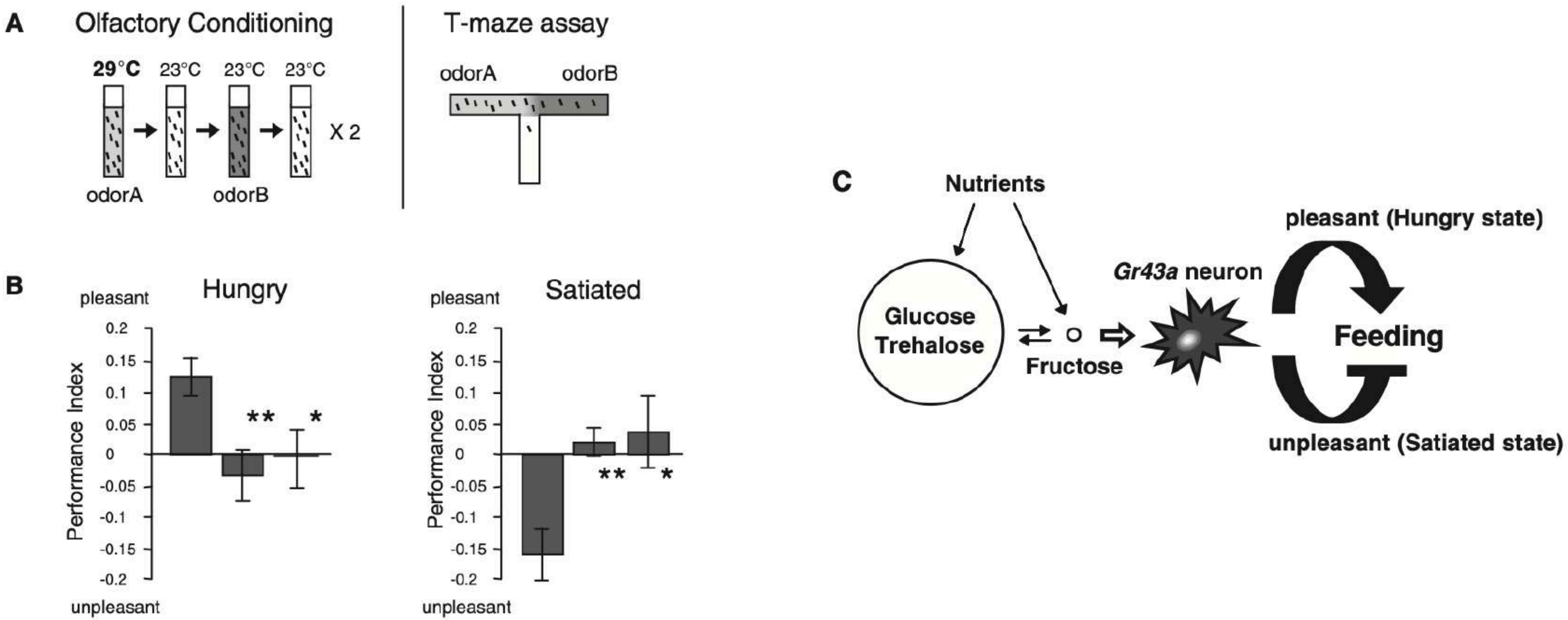


sweet, but nonnutritious



Miyamoto T, Slone J, Song X, et al. Cell, 2012.

Activation of Gr43a brain neurons evokes opposite, satiety-dependent valence

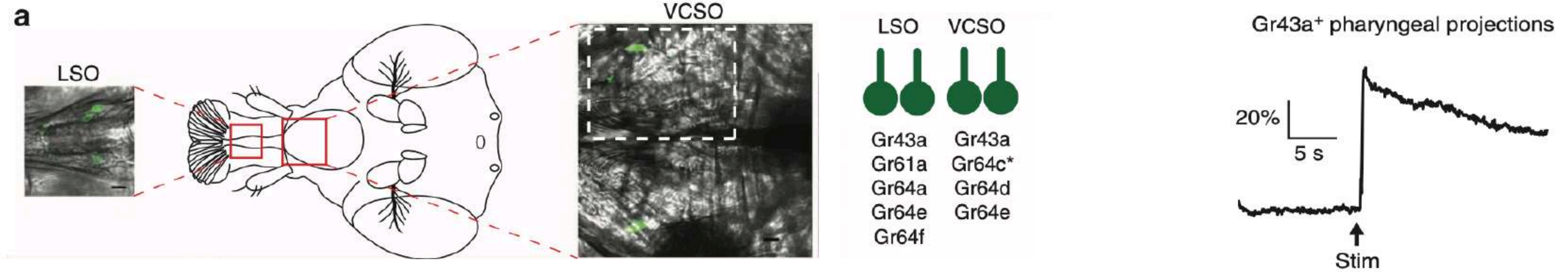


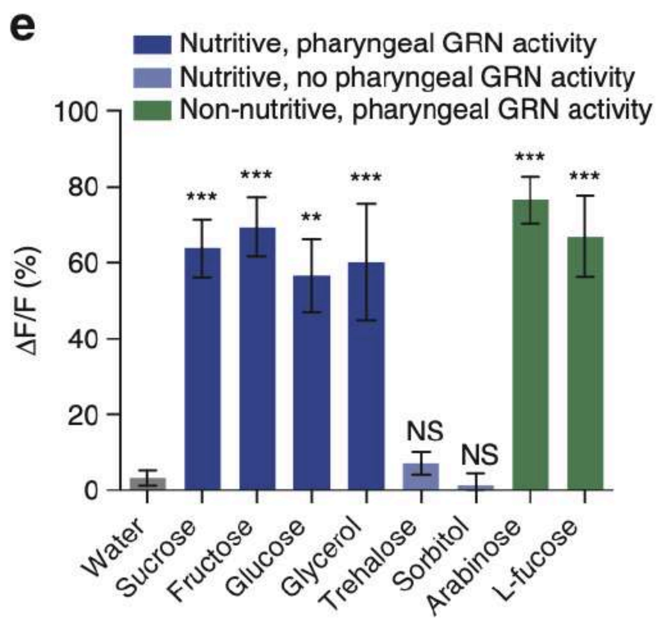
Gr43a^{GAL4}	+	+	−
Cha$^{7.4kb}$*-GAL80*	+	+	−
UAS-trpA1	+	−	+

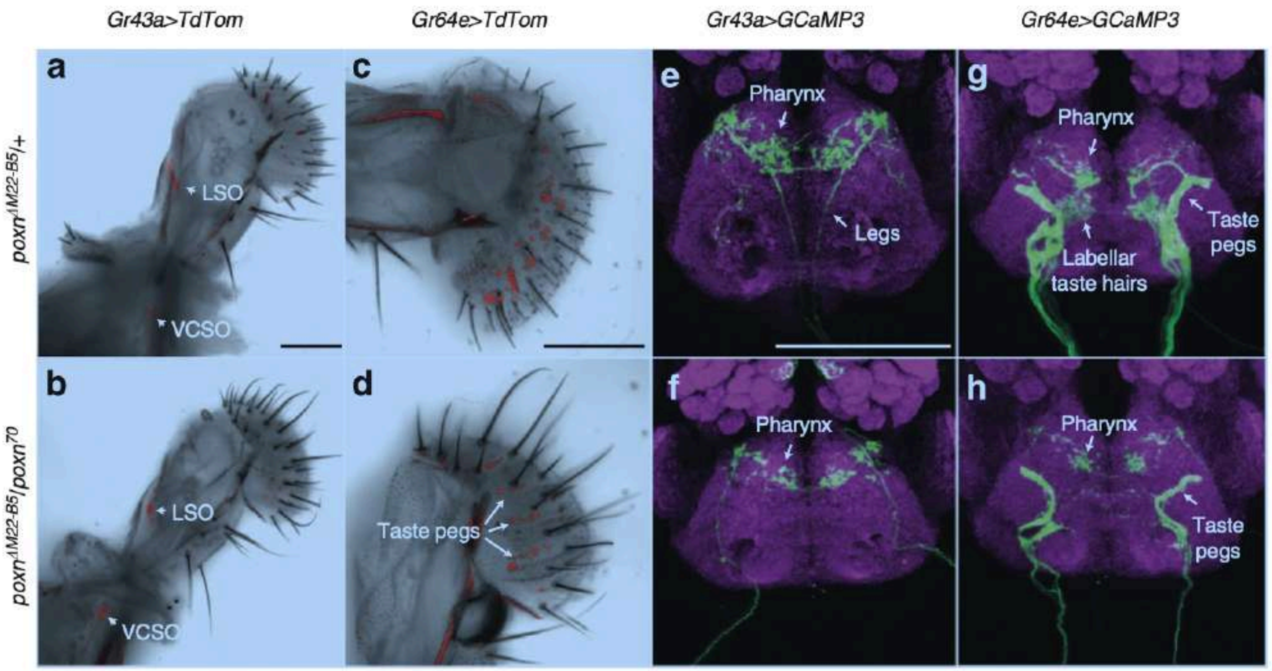
Gr43a^{GAL4}	+	+	−
Cha$^{7.4kb}$*-GAL80*	+	+	−
UAS-trpA1	+	−	+

Miyamoto T, Slone J , Song X , et al. Cell, 2012.

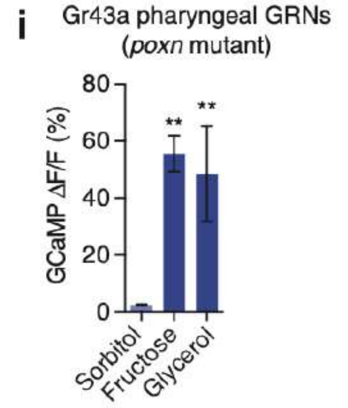
Pharyngeal GRNs are activated by the ingestion of sweet compounds

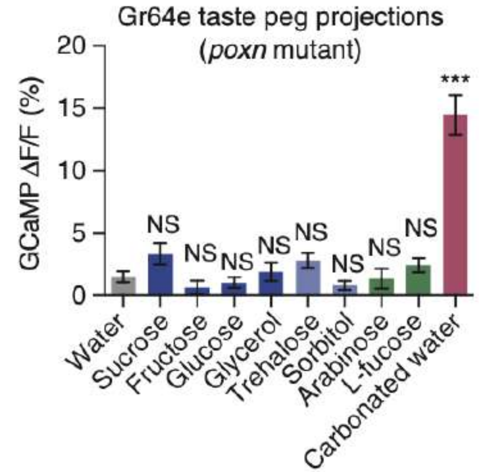






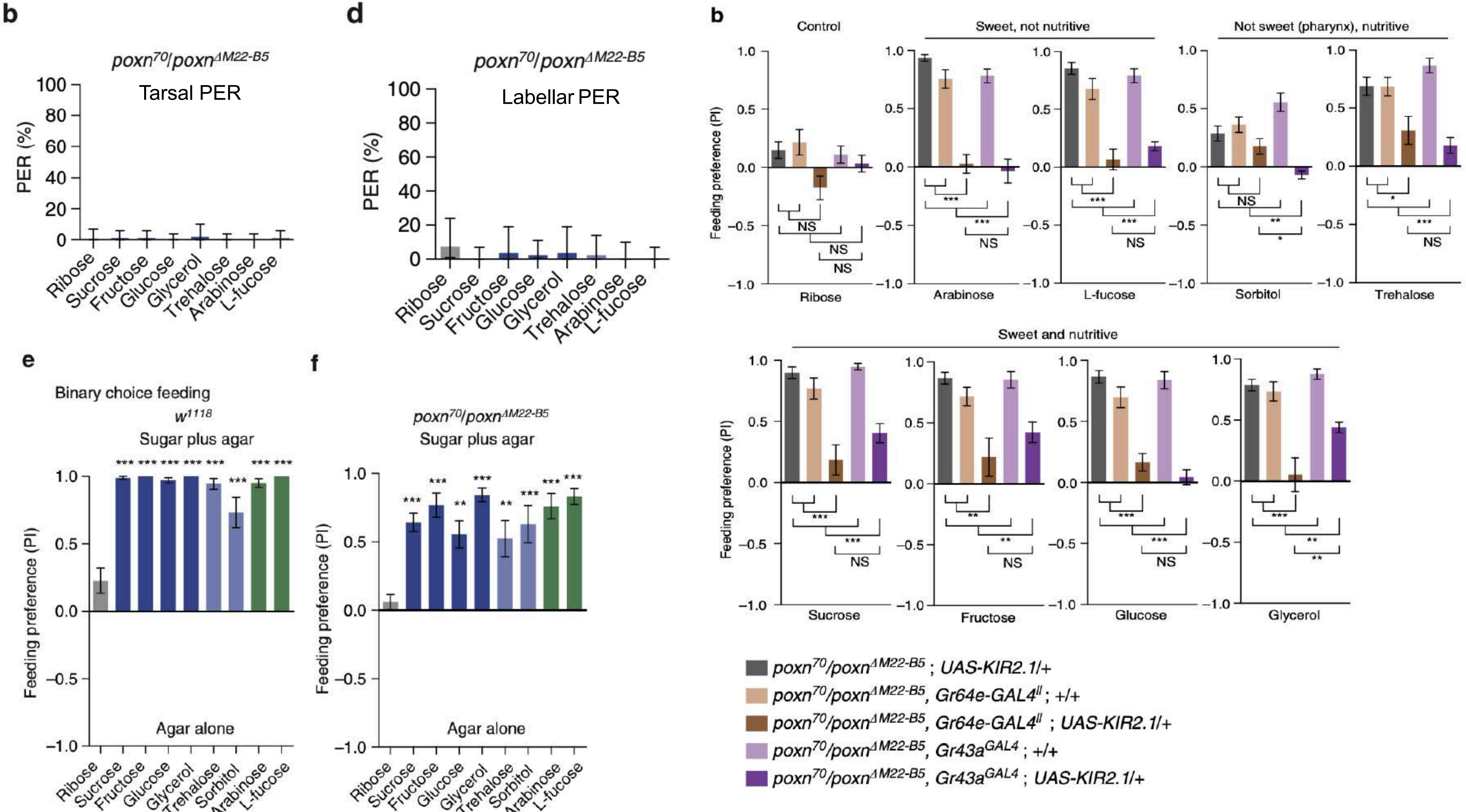
poxn mutants





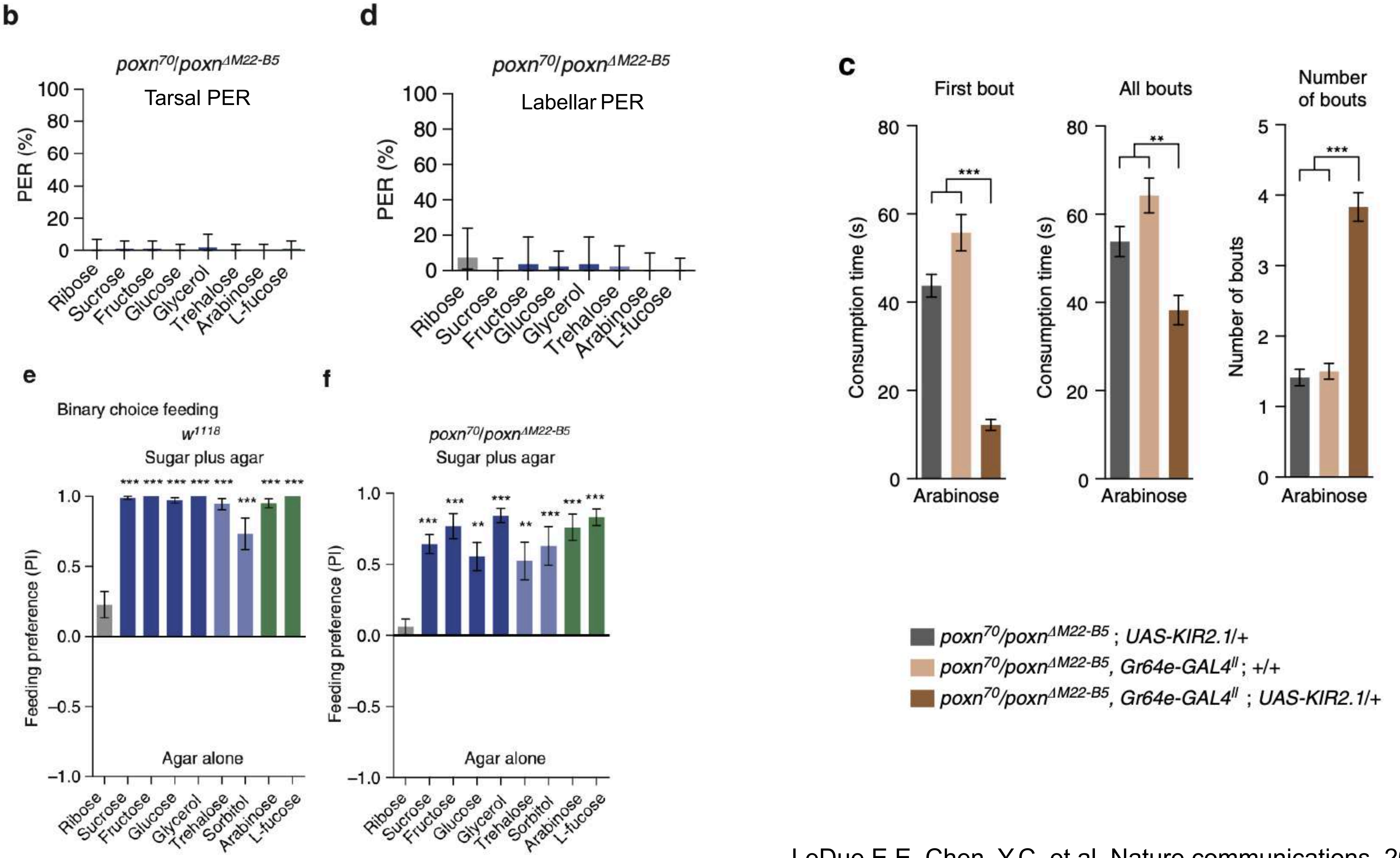
LeDue E.E, Chen Y.C, et al. Nature communications. 2015

Pharyngeal GRNs are necessary for the preference of poxn mutants for sweet compounds



LeDue E.E, Chen Y.C, et al. Nature communications. 2015

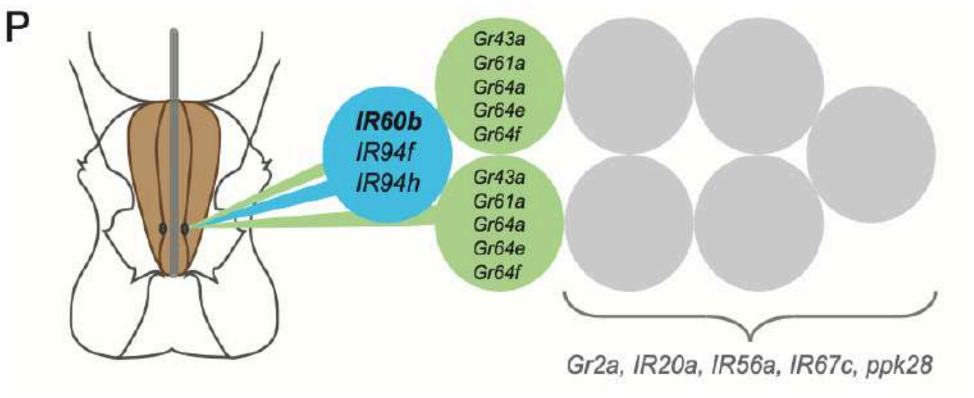
Pharyngeal GRNs indeed function to sustain ingestion of sweet food

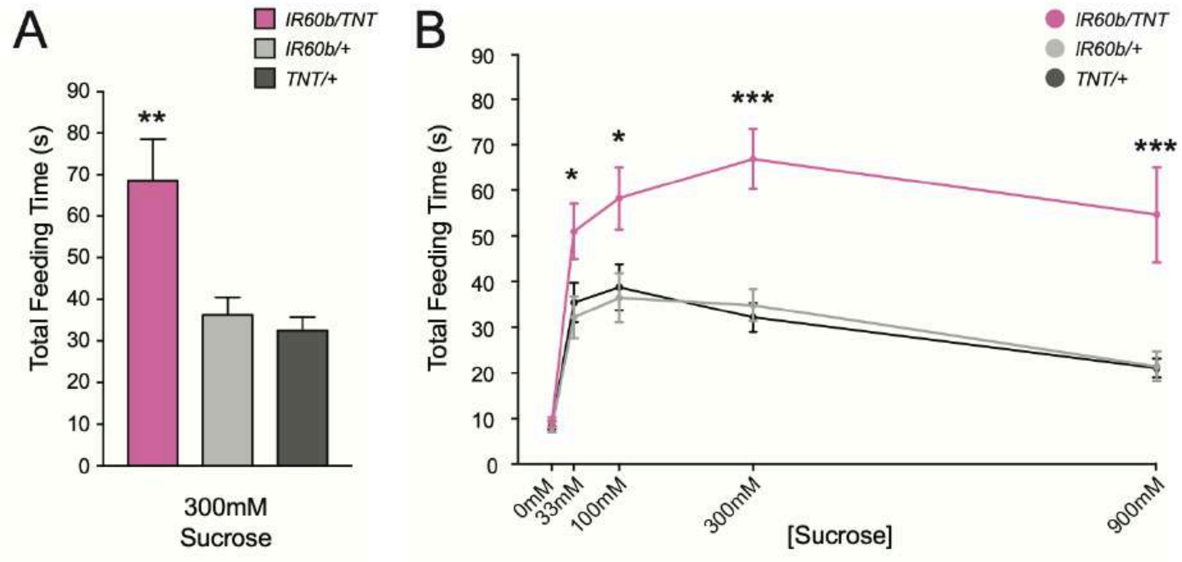


LeDue E.E, Chen Y.C, et al. Nature communications. 2015

IR60b neuron negatively regulates ingestion in response to sucrose

LSO sensillum 7





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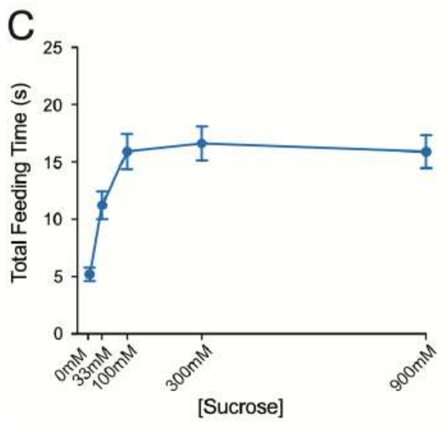
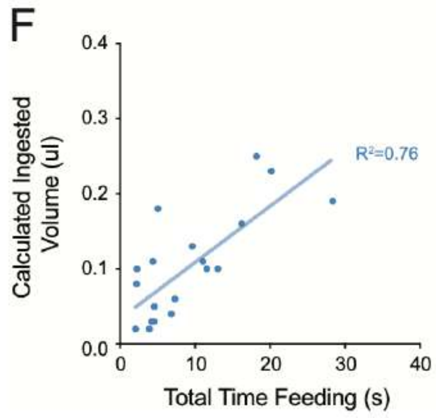
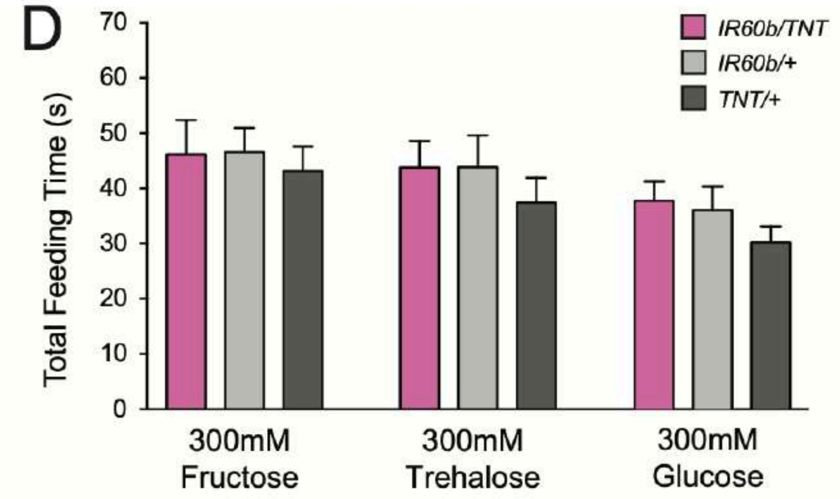
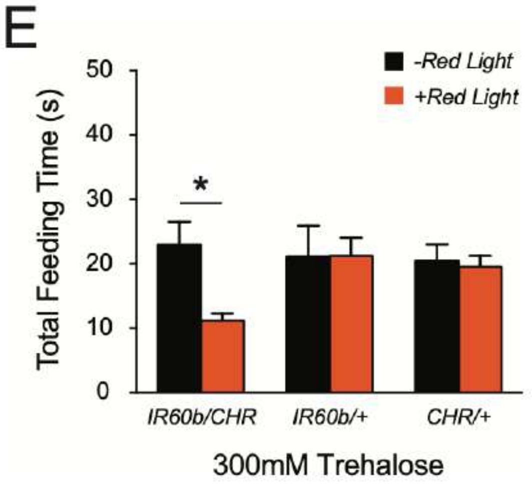


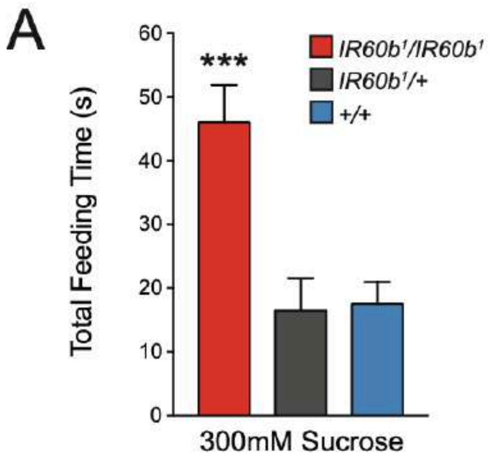


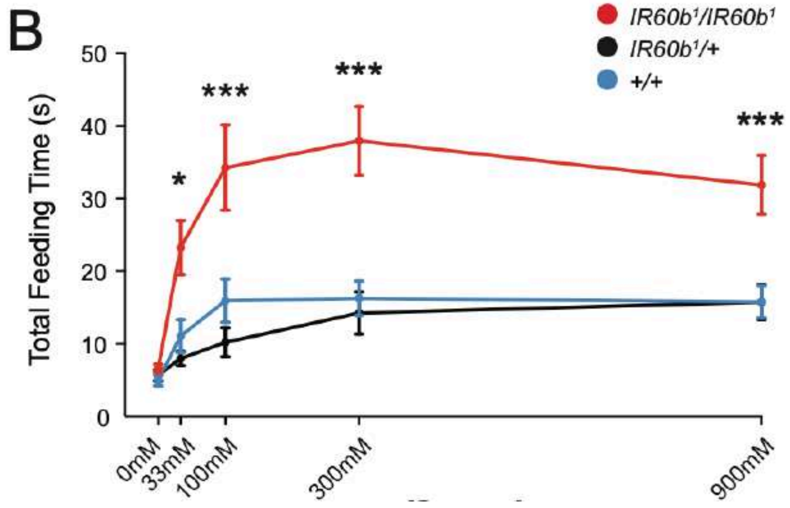


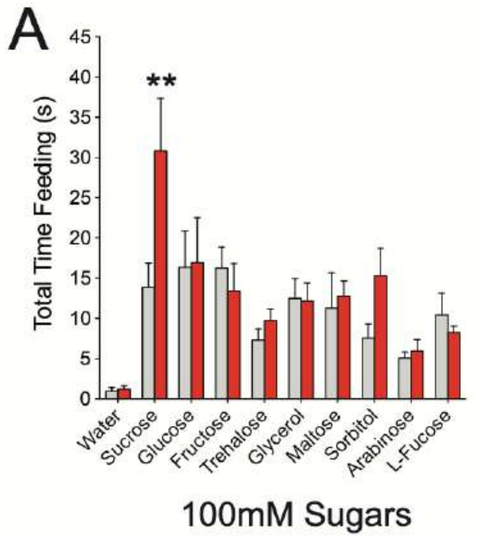


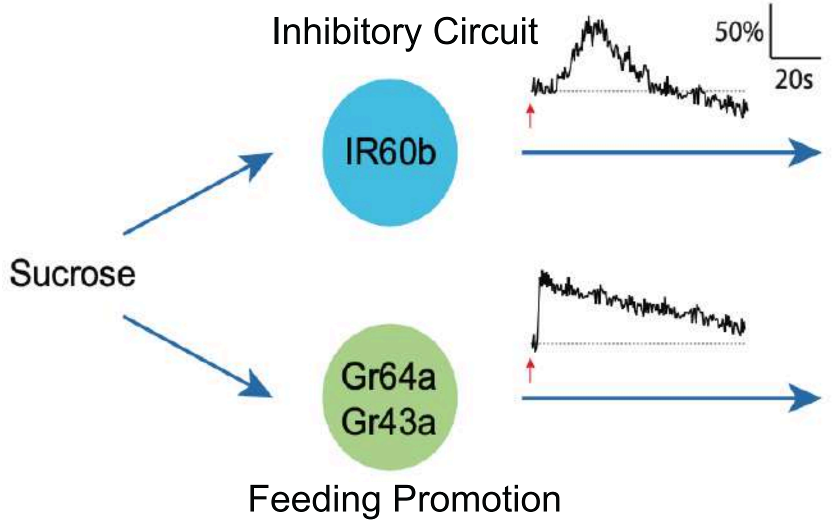
Joseph R M , Sun J S , Edric T , et al. eLife, 2017.

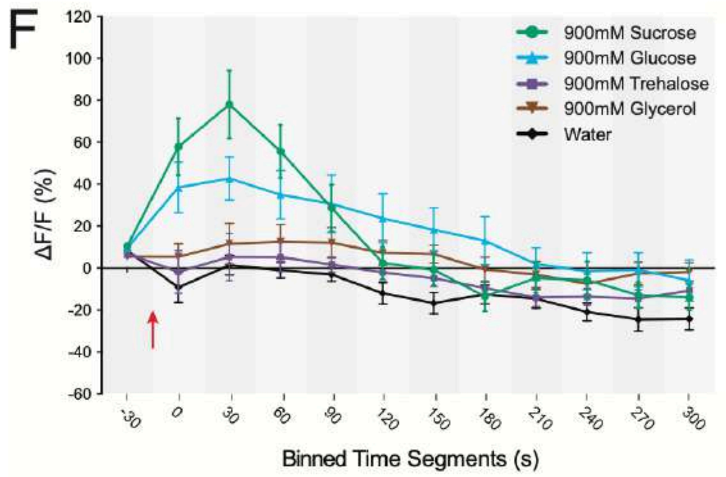
The IR60b neuron responds to sucrose depending on IR60b receptor

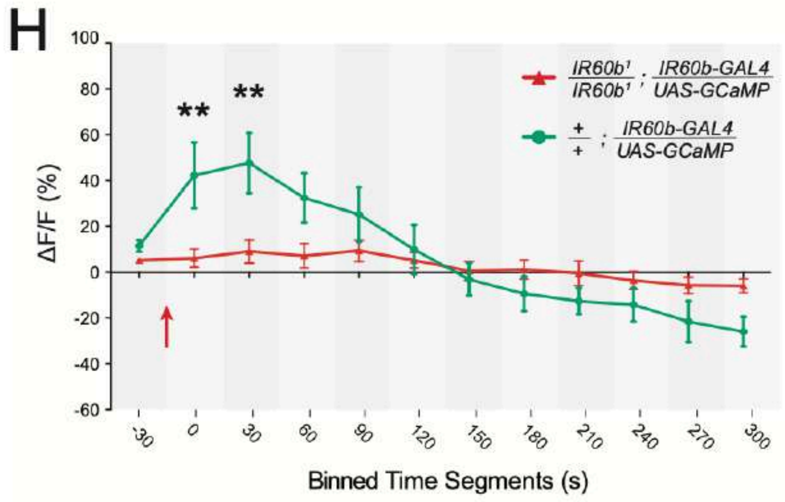






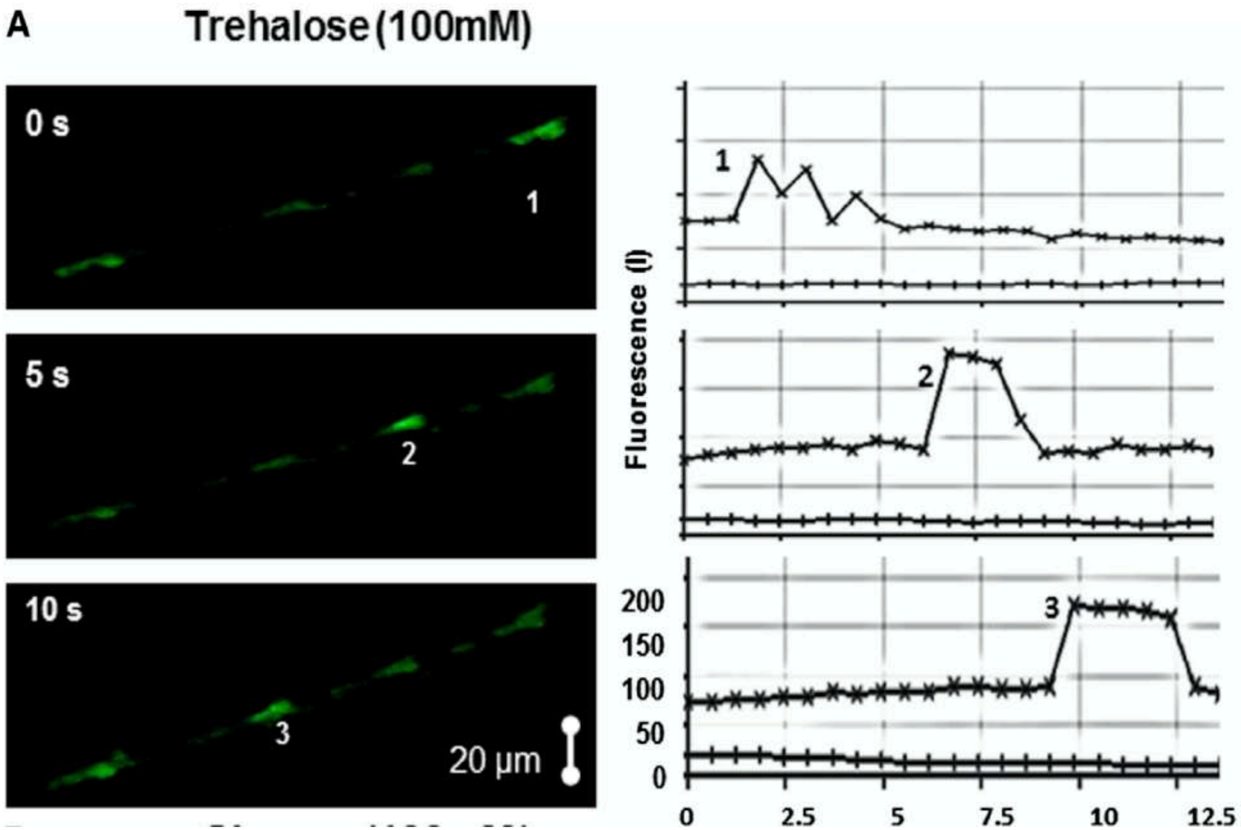


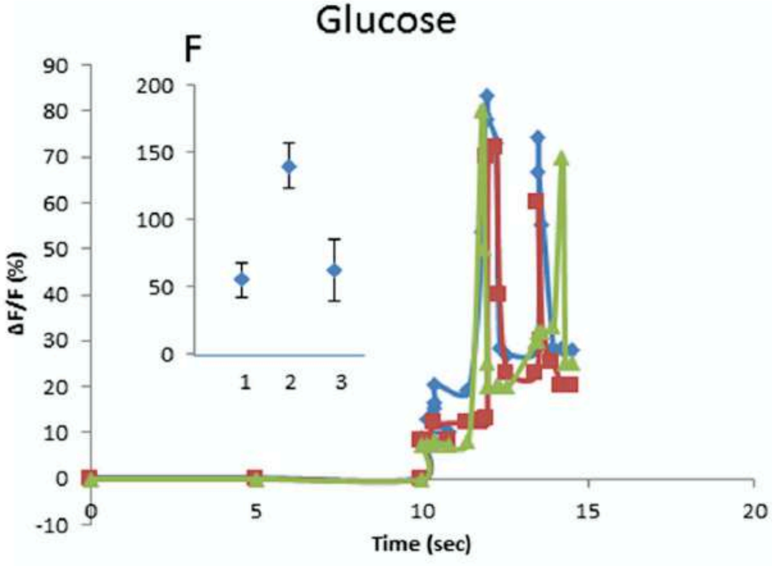


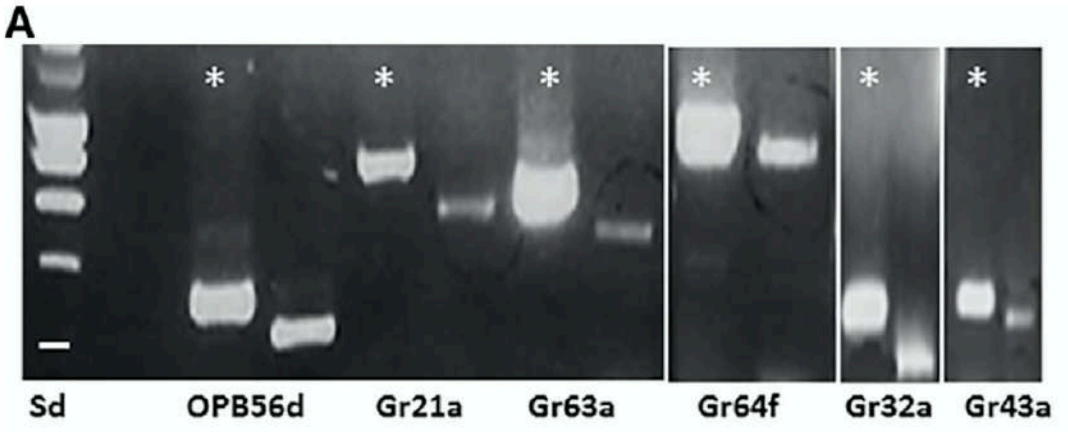


Joseph R M , Sun J S , Edric T , et al. eLife, 2017.

The wings of fly detect tastant cues from the environment by taste receptors

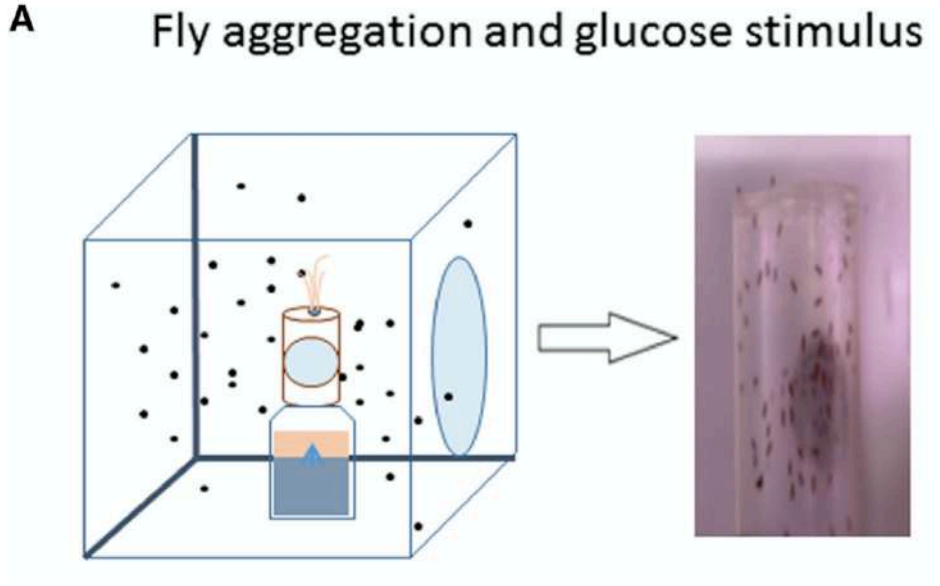


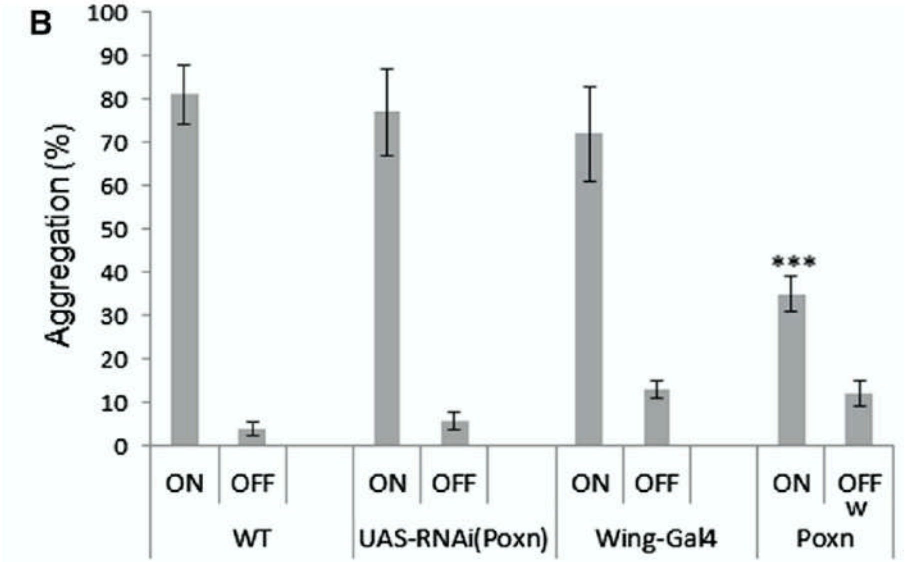


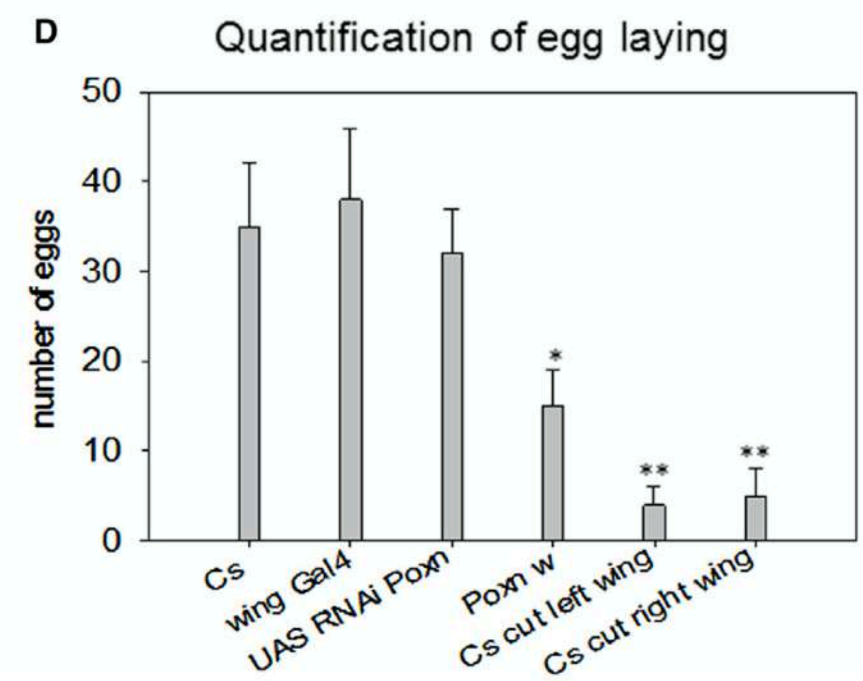


Raad H, Ferveur JF, Ledger N, et al. Cell Reports, 2016.

Taste sensilla knockdown in the wing abolishes aggregation and significantly reduces the number of eggs







Raad H, Ferveur JF, Ledger N, et al. Cell Reports, 2016.

Take-home Message

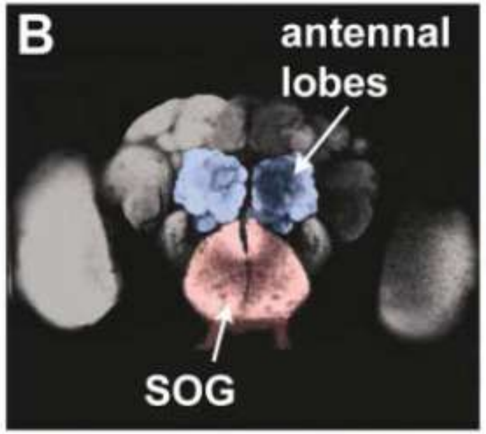
1. Gr5a is essential for trehalose sensation and is expressed in most sugar-responsive GRNs, while Gr64a, is required for detecting sucrose, maltose, and glucose.
2. Gr64f is a broadly required receptor for both Gr5a and Gr64a to detect sugar.
3. Individual sweet Grs are required for sensing multiple sugars, and each sugar response appears to be dependent on multiple sweet Grs.
4. Gr43a is a fructose receptor and functions as a nutrient sensor for hemolymph fructose.
5. Gr43a pharyngeal GRNs detect sustained consumption of sweet compounds, while IR60b neurons inhibit sucrose consumption.
6. The wing GRNs are involved in the process of chemical detection.

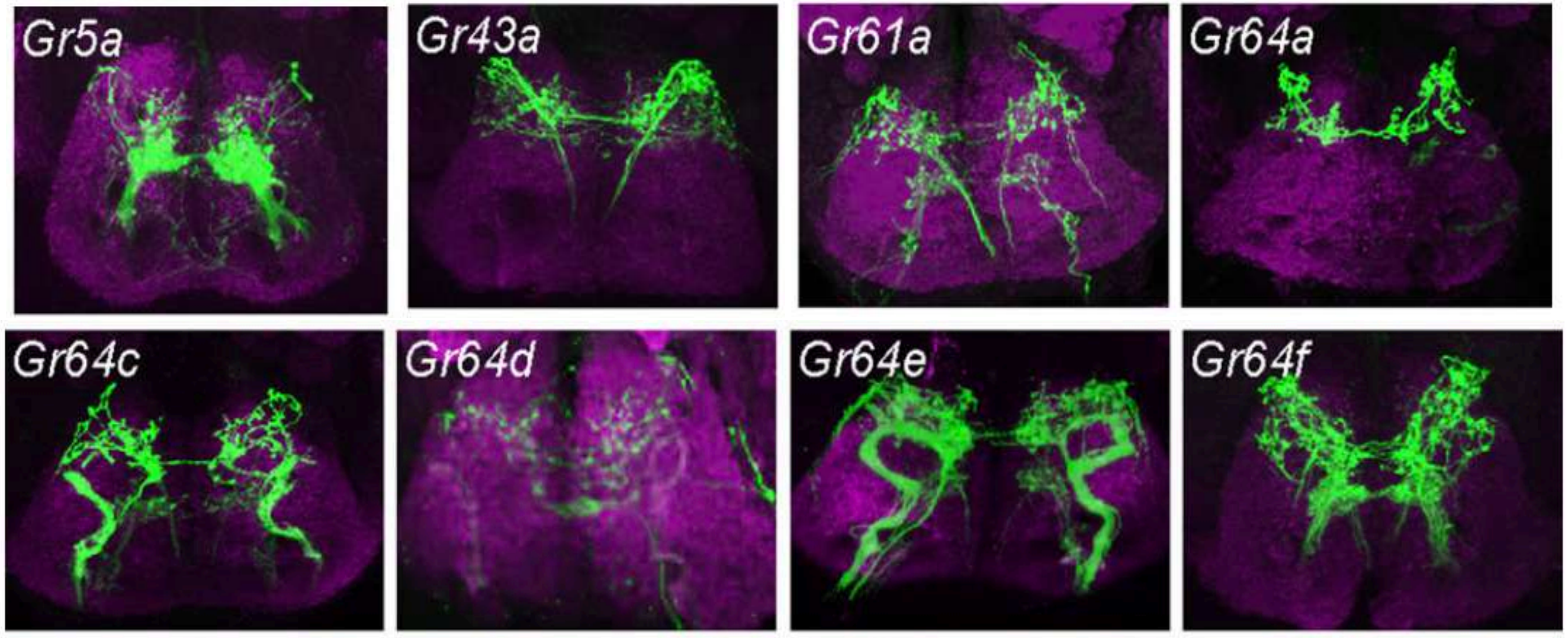
TWO.

Sweet Taste Processing In The Brain

SMS

sweetness gustatory neurons projections in the SOG：

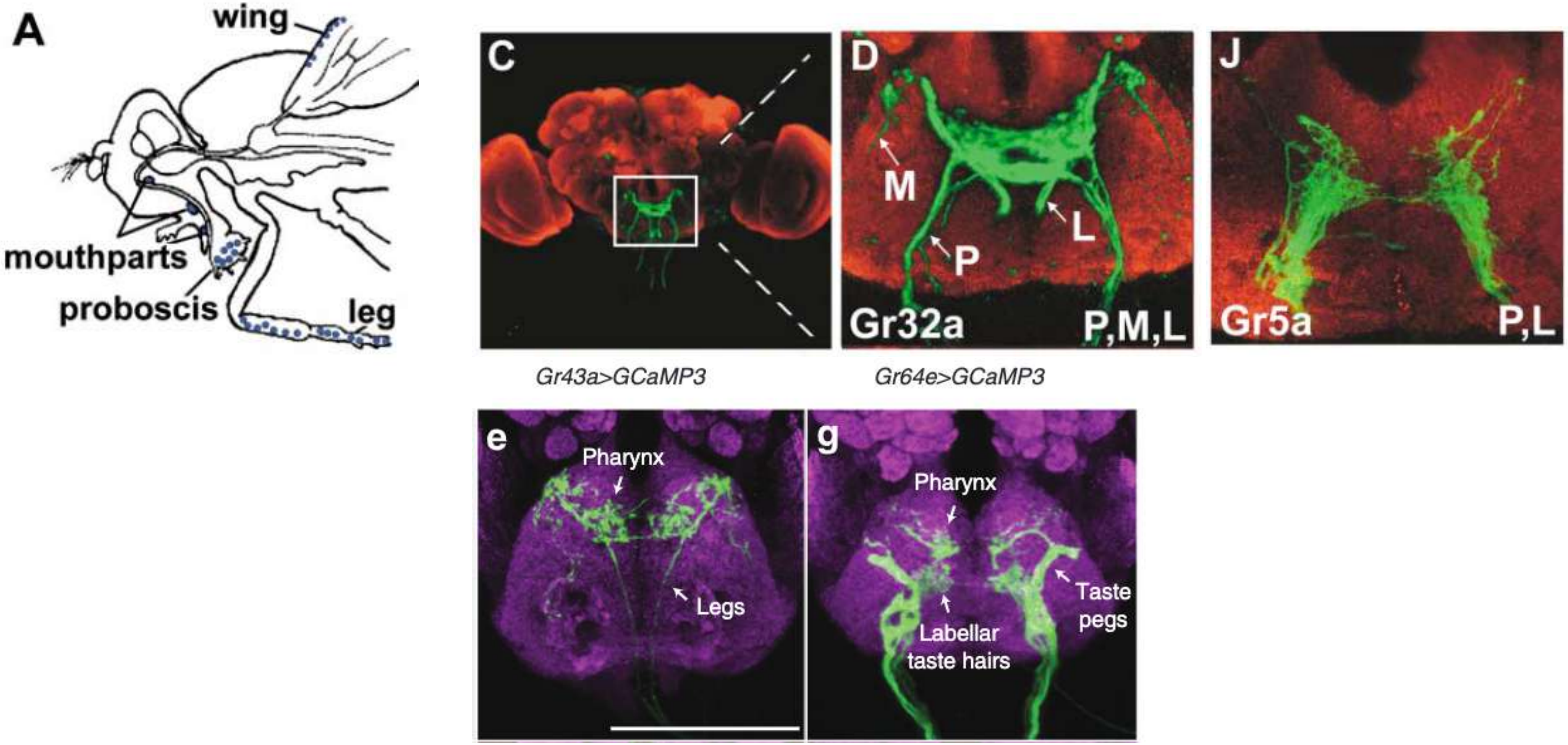




subesophageal ganglion (SOG): the first relay center of taste processing in the brain

J. Y. Kwon, A. Dahanukar, L. A. Weiss, J. R. Carlson, J Biosciences. 39, 565–574 (2014).
Z. Wang, A. Singhvi, P. Kong, K. Scott, Cell. 117, 981–991 (2004).

Taste neurons in different tissues project to different locations in the SOG.



M: mouthparts
P: proboscis
L: leg

Z. Wang, A. Singhvi, P. Kong, K. Scott, Cell. 117, 981–991 (2004).
E. E. LeDue, Y.-C. Chen, A. Y. Jung, A. Dahanukar, M. D. Gordon, Nature Communications. 6, 6667 (2015).

ARTICLE

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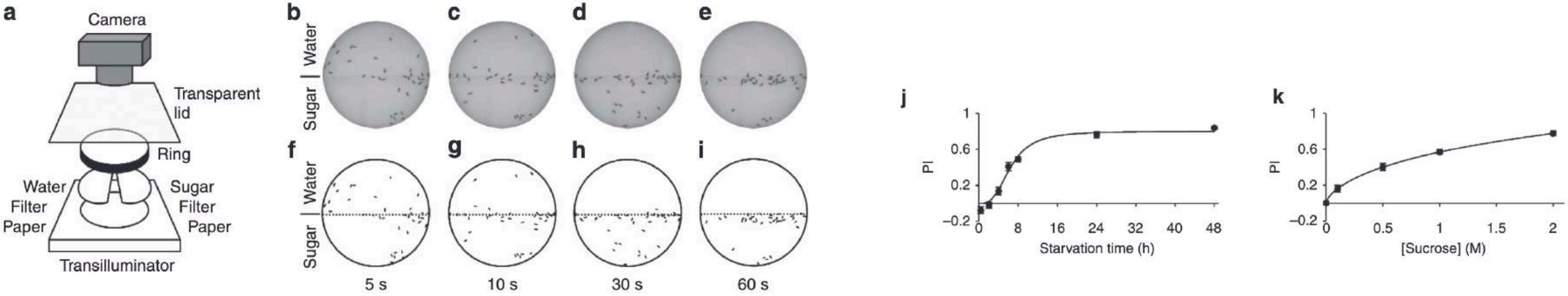
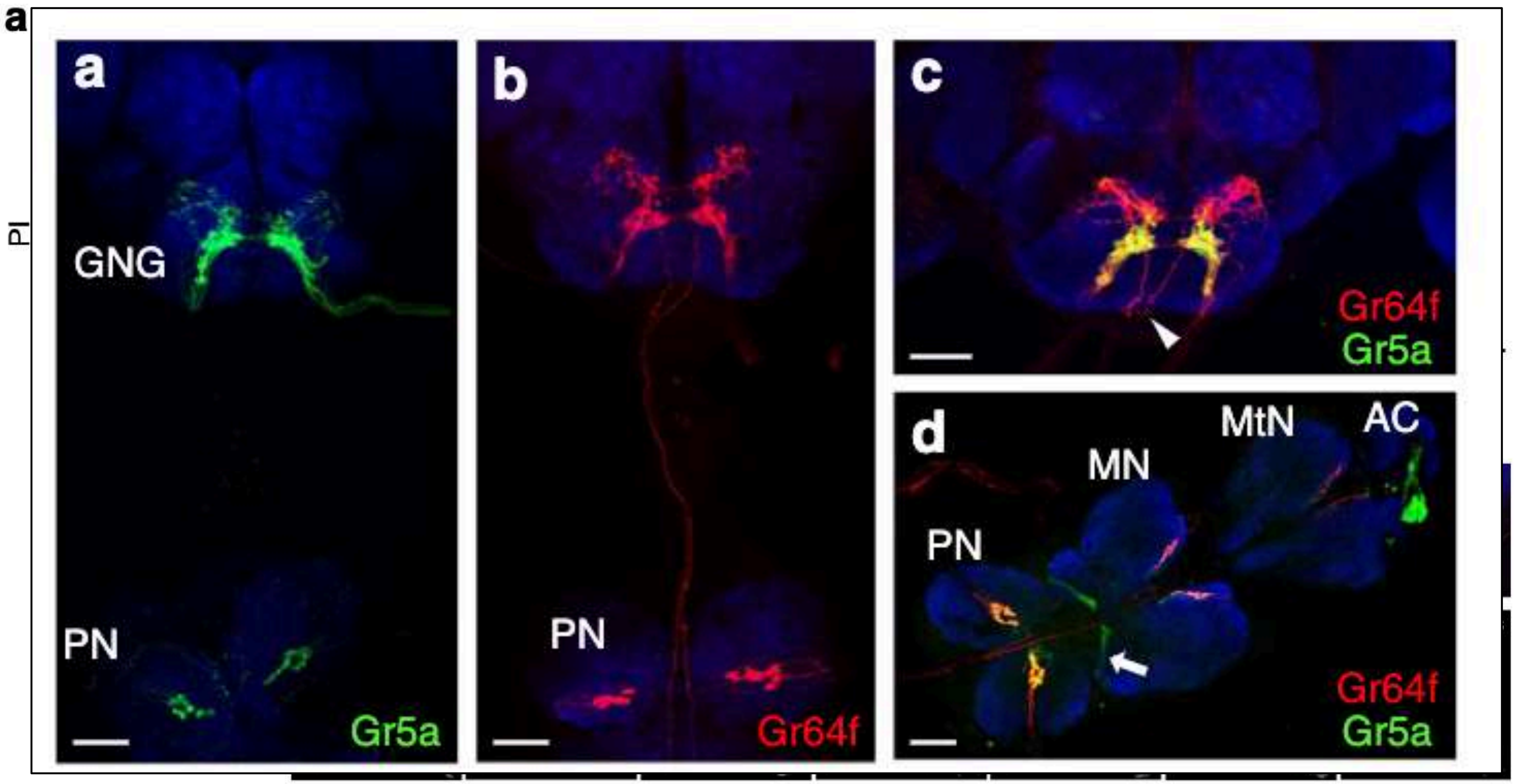
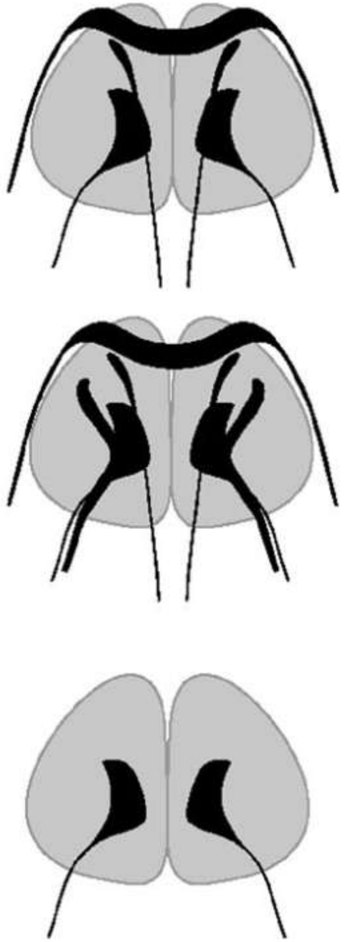
Functional dissociation in sweet taste receptor neurons between and within taste organs of *Drosophila*

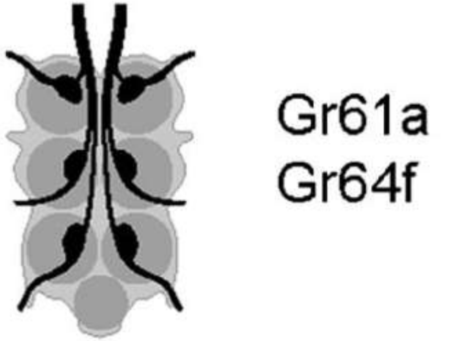
Vladimiros Thoma[1,2], Stephan Knapek[2], Shogo Arai[3], Marion Hartl[2,†], Hiroshi Kohsaka[4], Pudith Sirigrivatanawong[3], Ayako Abe[1], Koichi Hashimoto[3] & Hiromu Tanimoto[1,2]



sweet GRNs in the legs are required for sugar preference







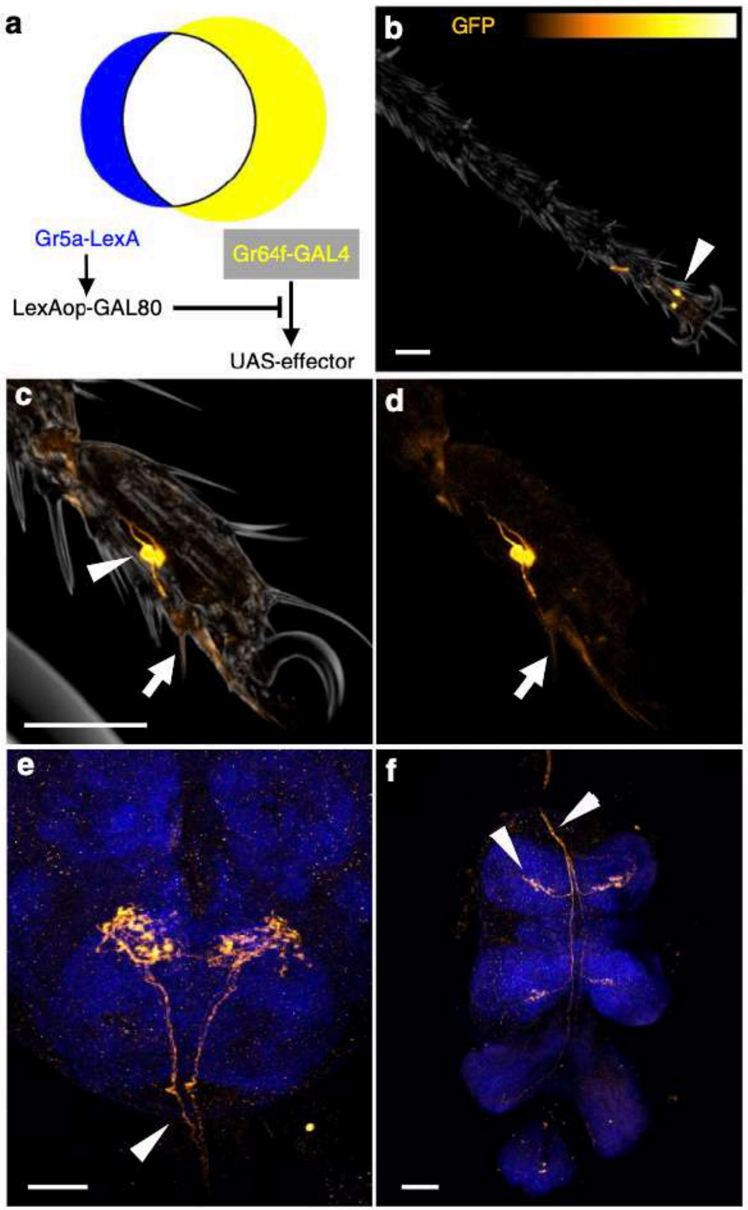
ascending tarsal GRNs, atGRNs

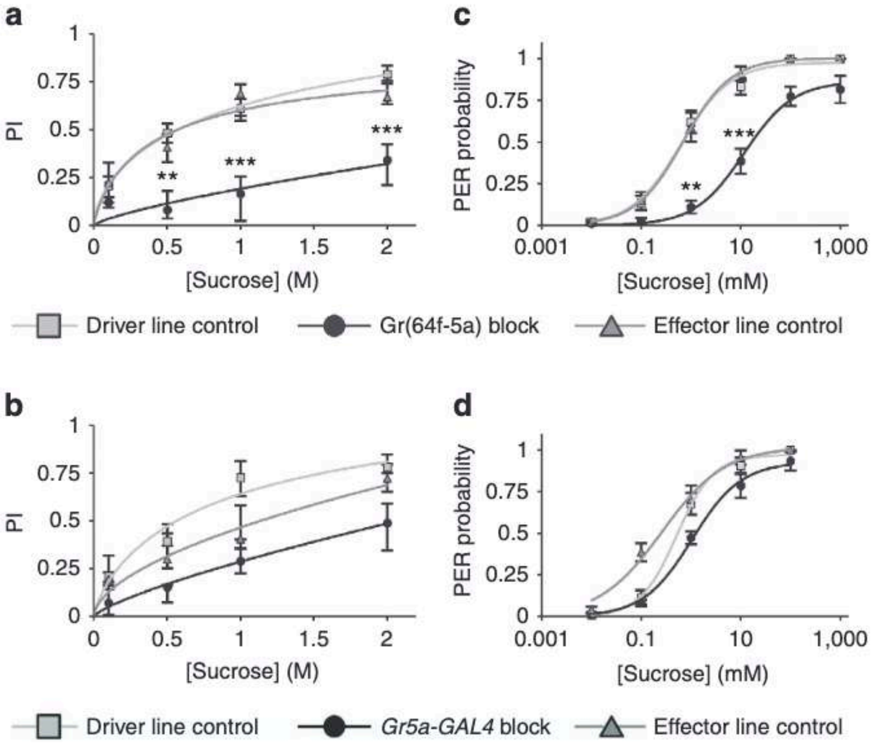
segmental tarsal GRNs, stGRNs

Kwon, J. Y., Dahanukar, A., Weiss, L. A. & Carlson, J. R. A map of taste neuron projections in the Drosophila CNS. J Biosciences 39, 565–574 (2014).

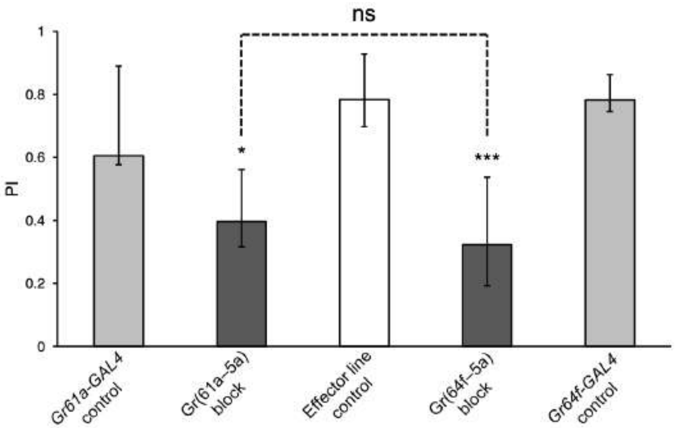
atGRNs are required for feeding initiation.

atGRNs: Gr(64f-5a)

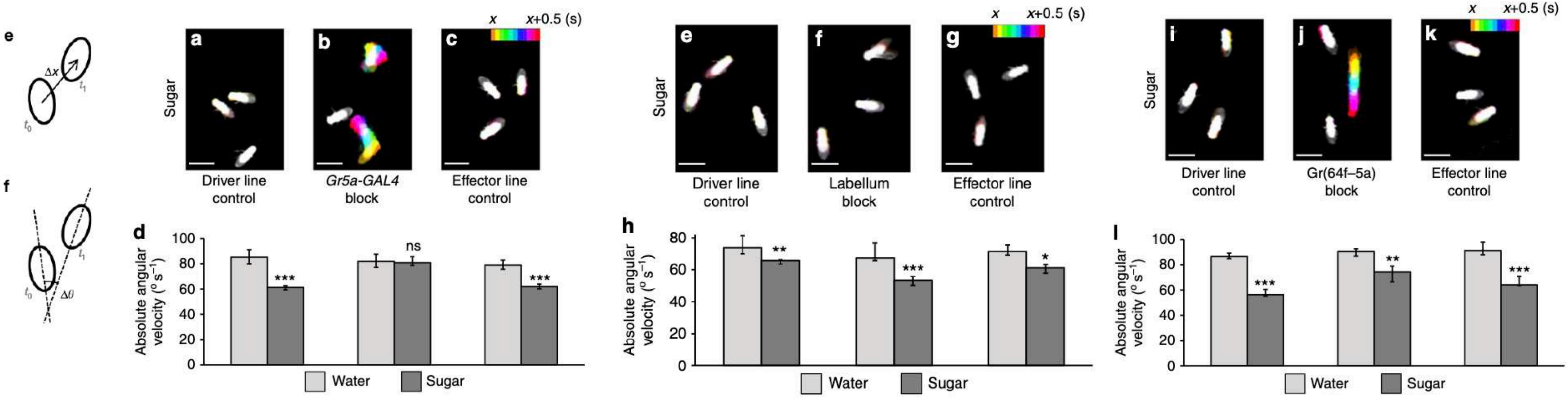




stimulation on tarsus



stGRNs are required for locomotion suppression.



- Functional dissociation of sweet taste receptor neurons in the tarsus.

atGRNs (terminate in brain SOG): feeding initiation

stGRNs (terminate in VNC): locomotion suppression upon food encounter

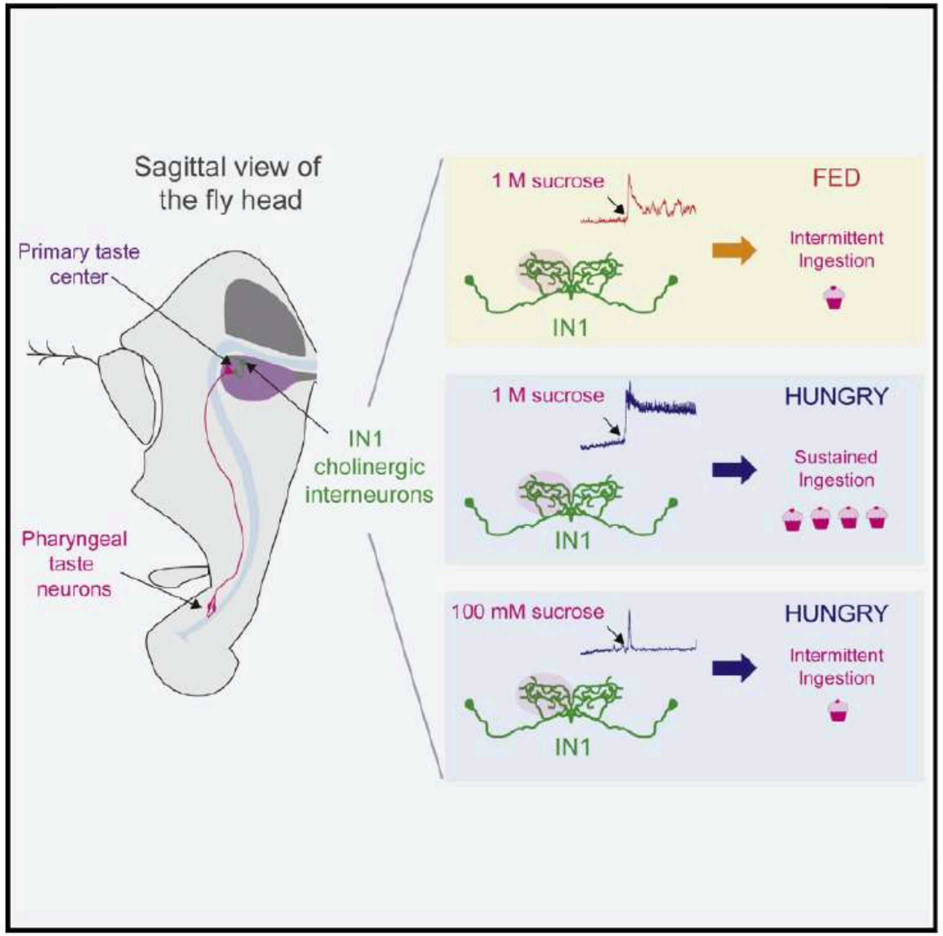
- Input from each taste organ is relayed to distinct higher-order neuronal circuits, which in turn regulate different aspects of feeding behavior.

Cell

Article

A Taste Circuit that Regulates Ingestion by Integrating Food and Hunger Signals

Graphical Abstract



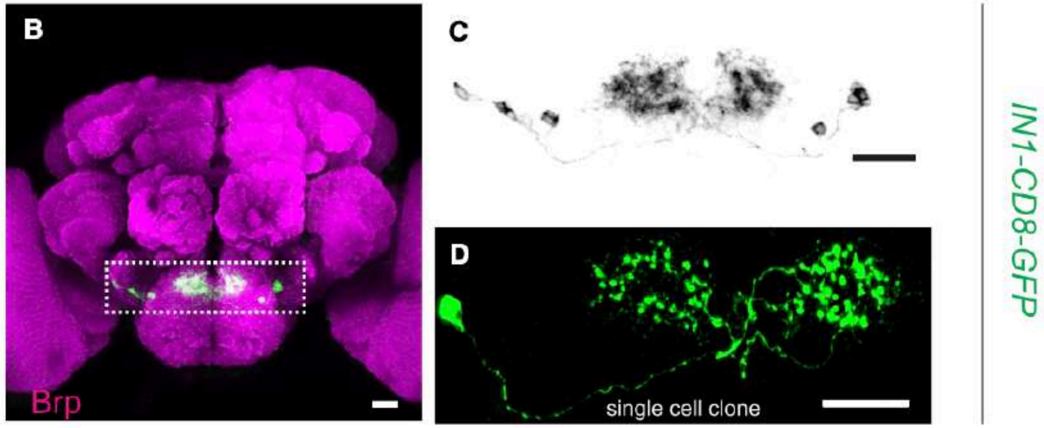
Authors

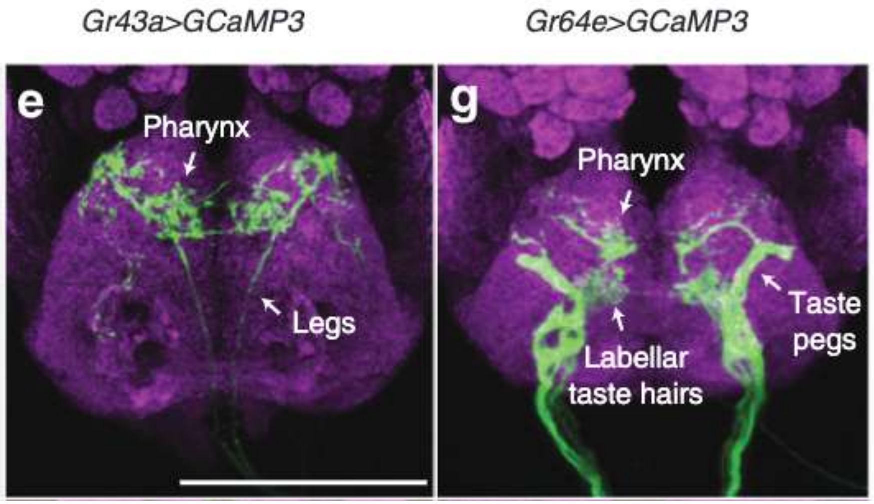
Nilay Yapici, Raphael Cohn, Christian Schusterreiter, Vanessa Ruta, Leslie B. Vosshall

Yapici et al., 2016, Cell *165*, 715–729

http://dx.doi.org/10.1016/j.cell.2016.02.061

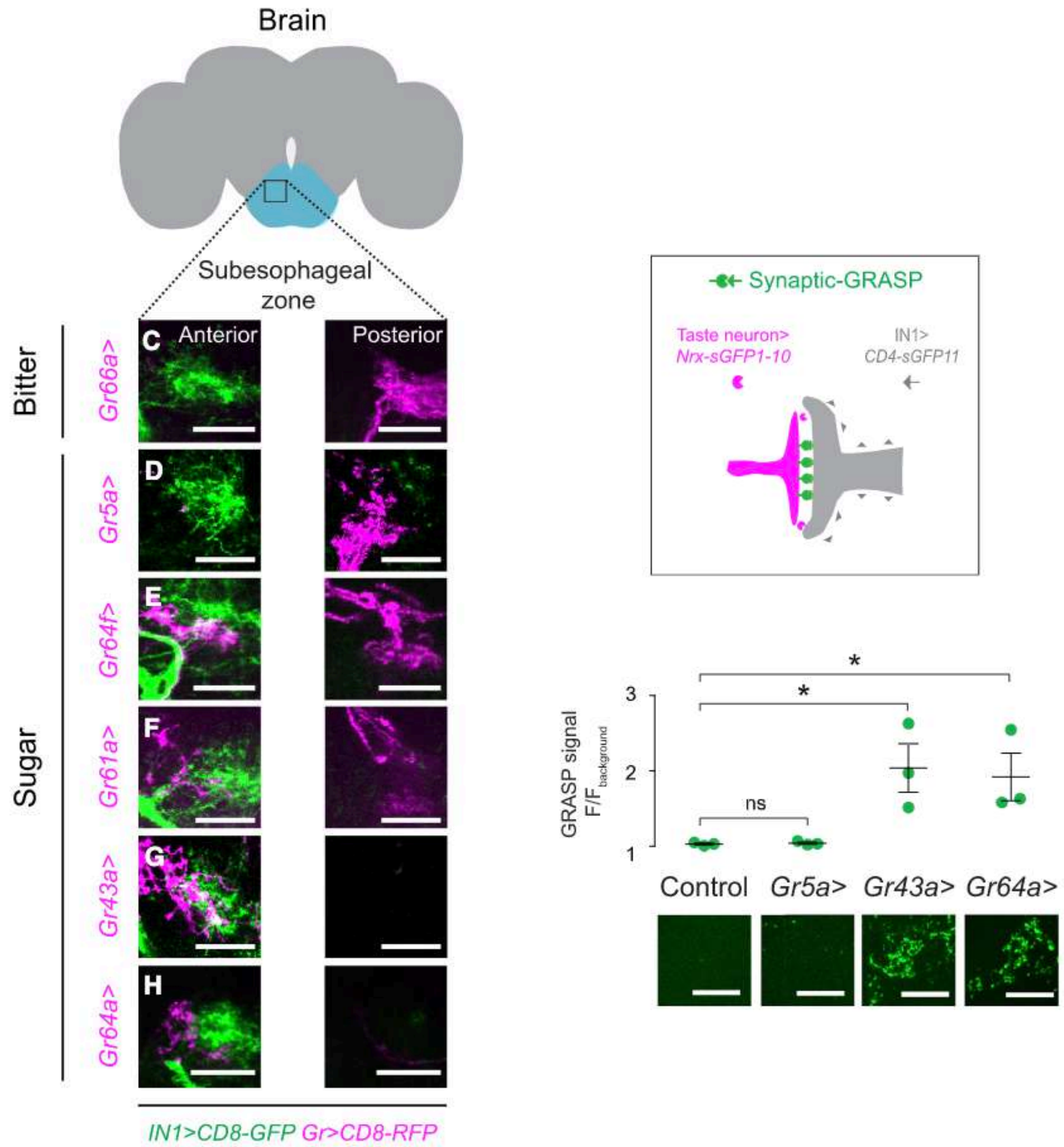
IN1 neurons



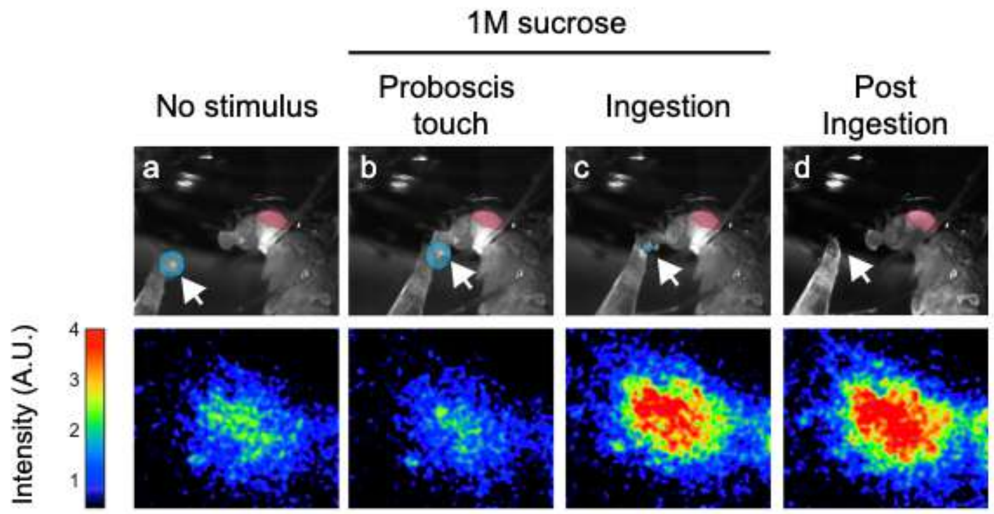


E. E. LeDue, Y.-C. Chen, A. Y. Jung, A. Dahanukar, M. D. Gordon, Nature Communications. 6, 6667 (2015).

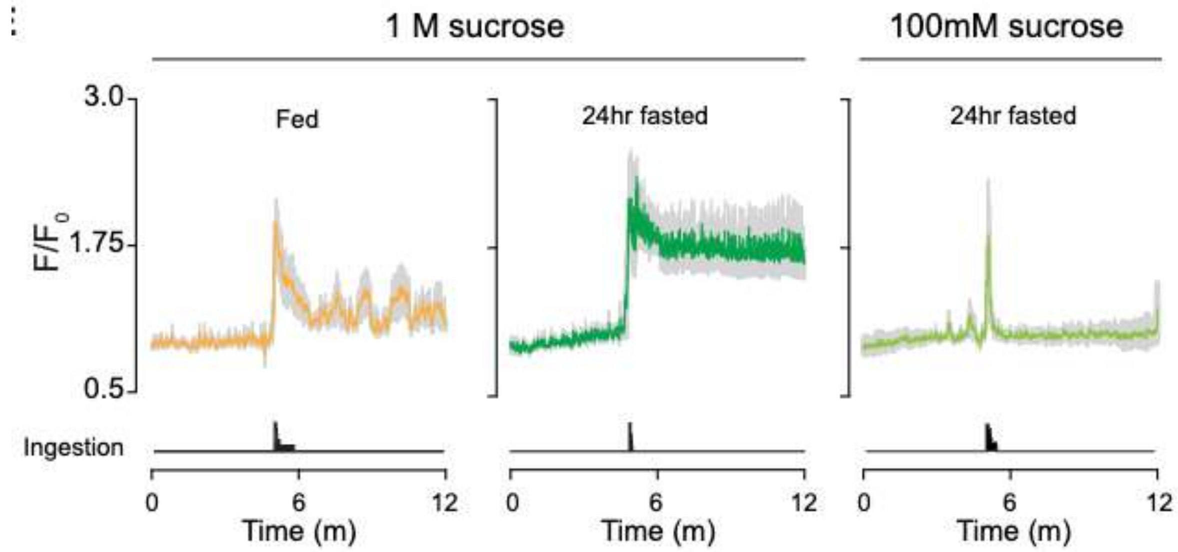
IN1 interneurons receive presynaptic input from sugar sensitive neurons in the pharynx.



IN1 neurons were strongly activated when sucrose was ingested.



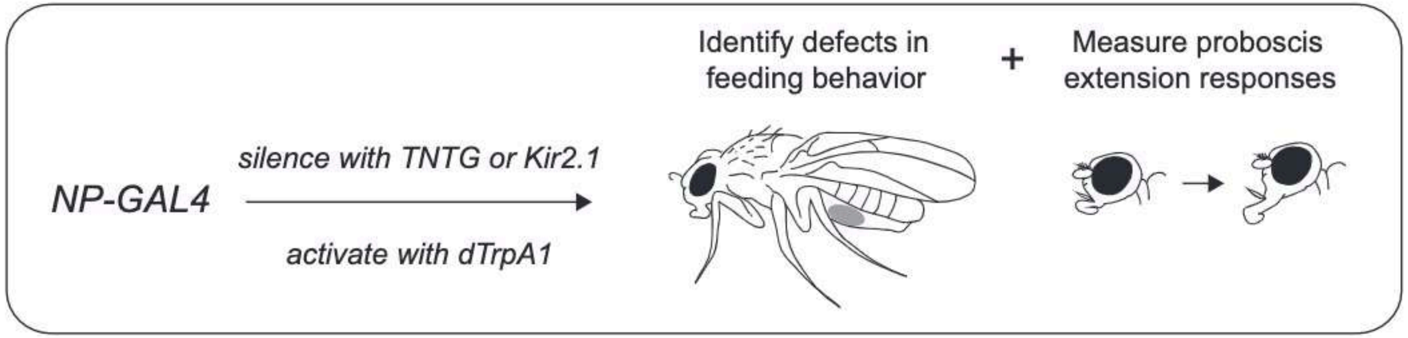
Hunger state and sucrose concentration modulate IN1 activity.

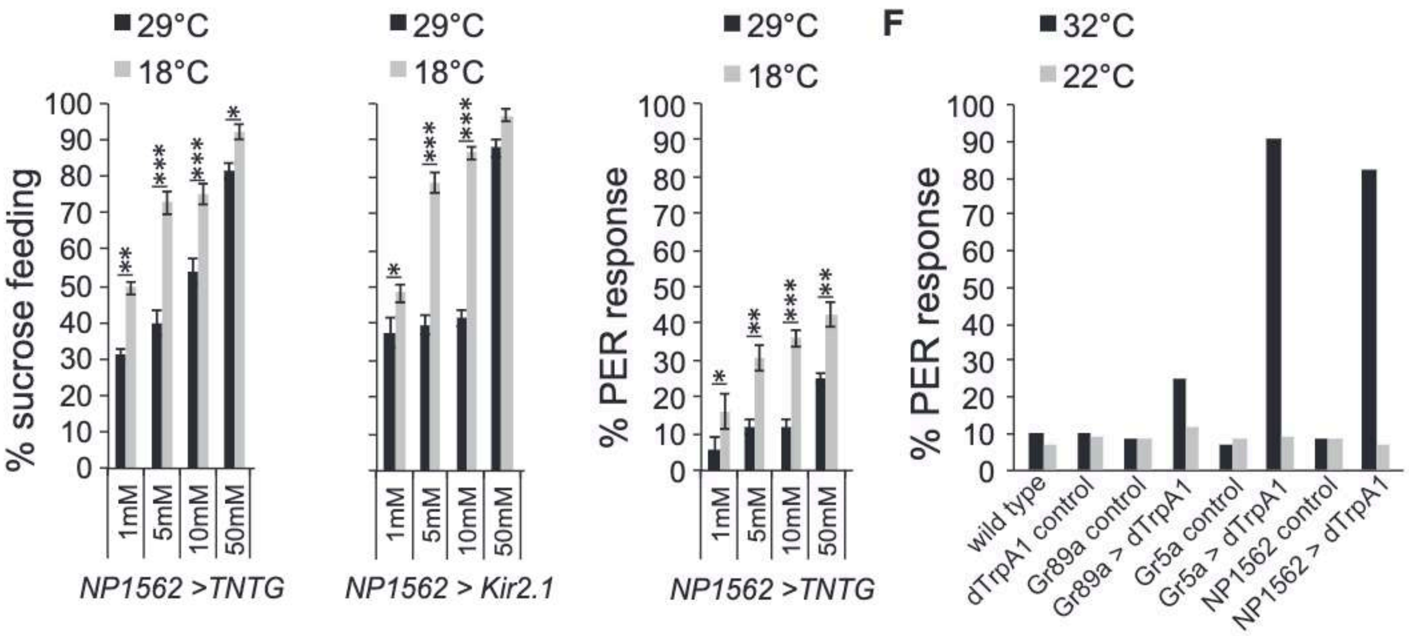


Article

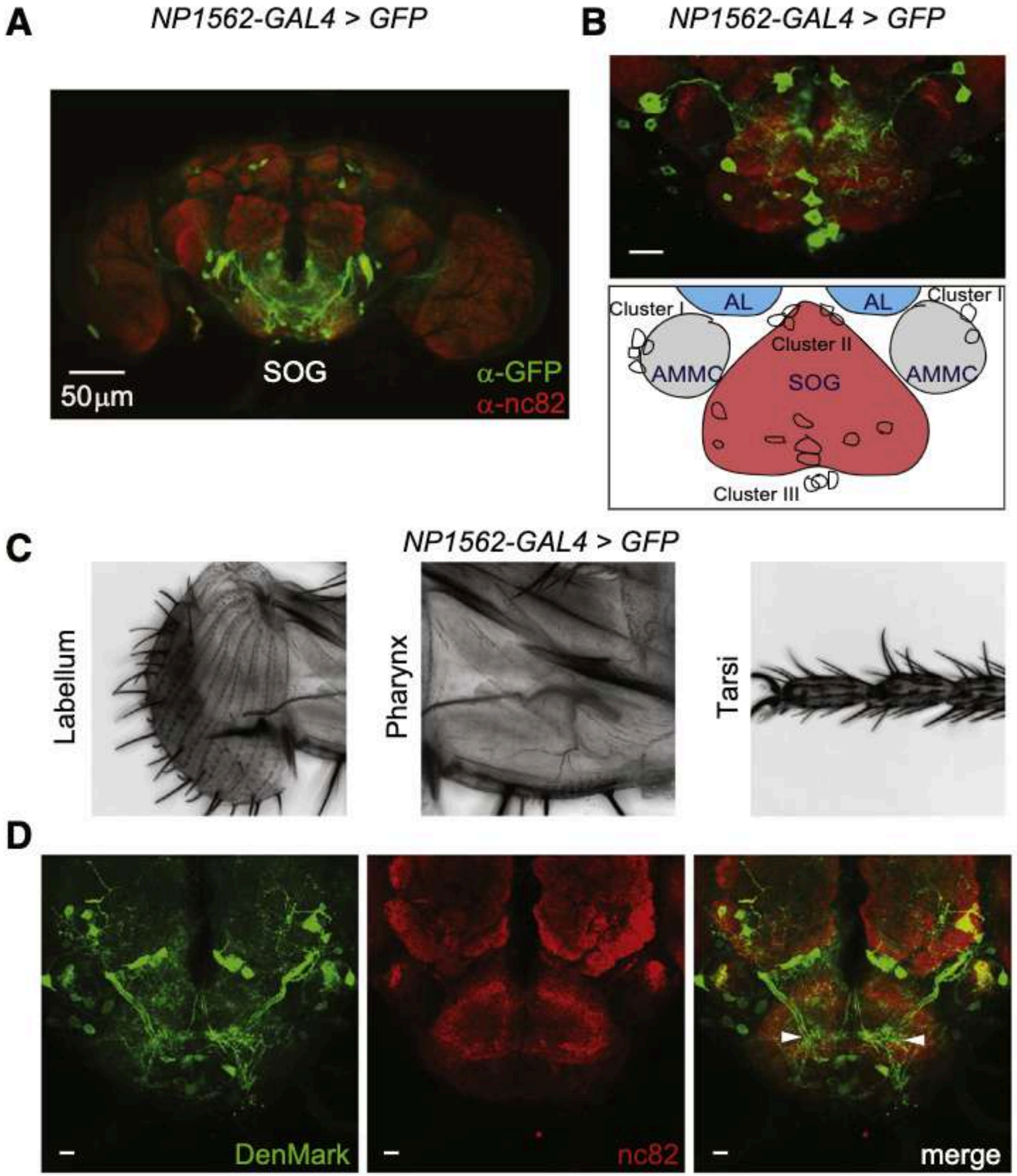
Neuron

Secondary Taste Neurons that Convey Sweet Taste and Starvation in the *Drosophila* Brain

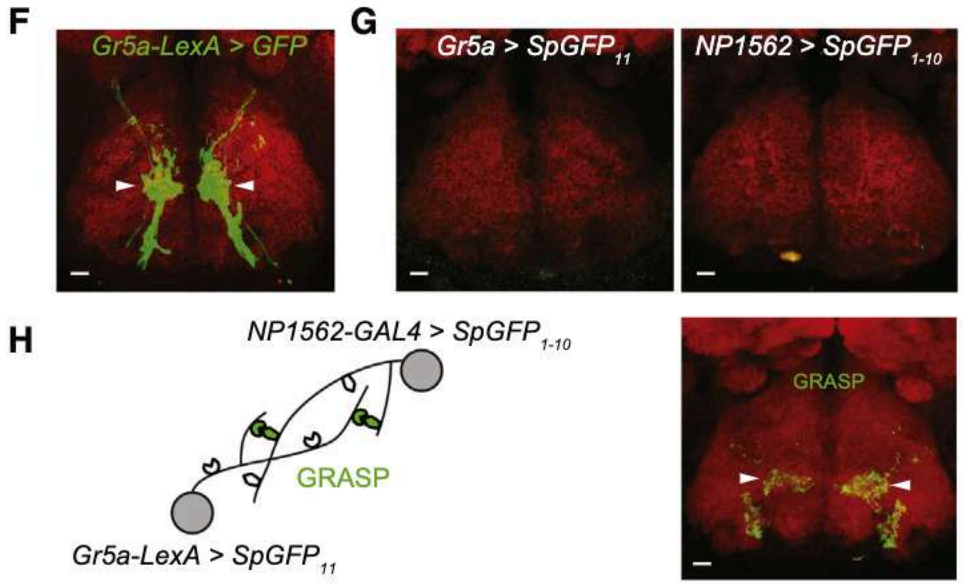




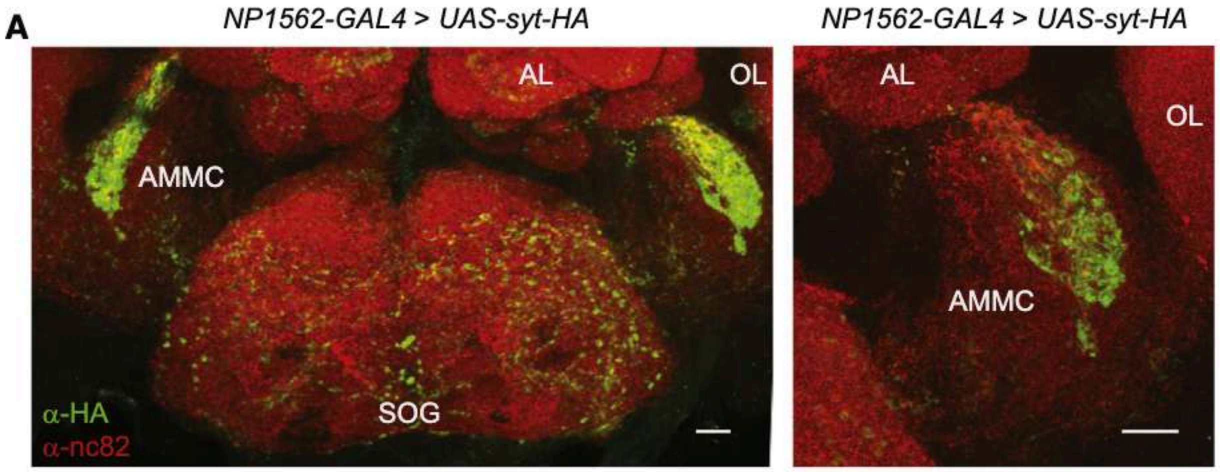
NP1562 Neurons send dendrites to the sweet taste region of the SOG



NP1562 neurons GRASP with Gr5a+ neurons in the SOG

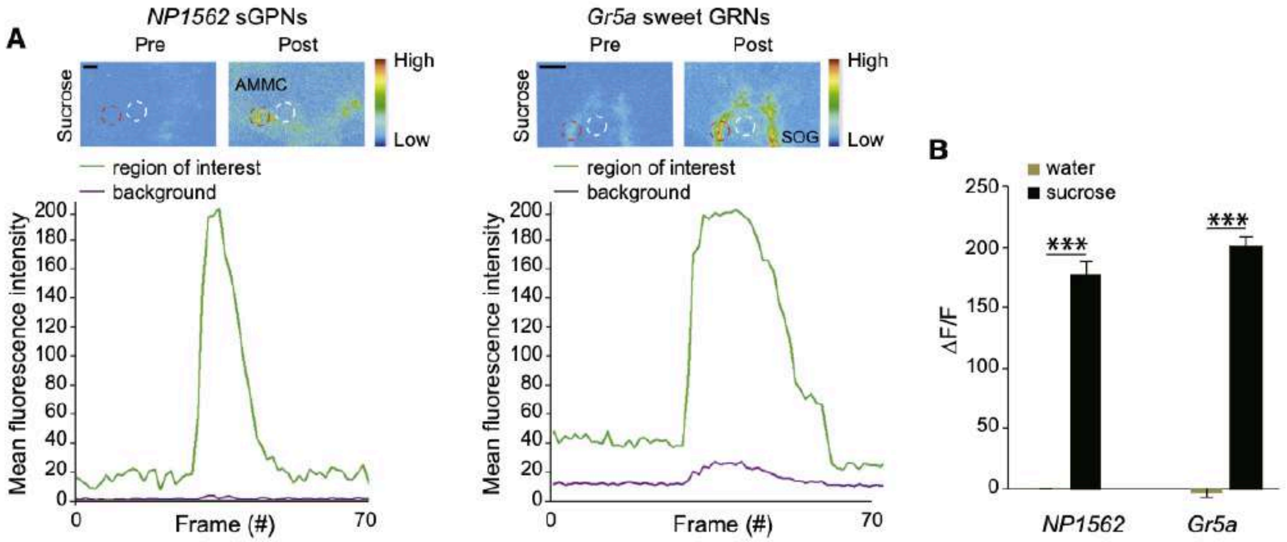


pre-synaptic terminals of NP1562-GAL4 neurons locate in AMMC

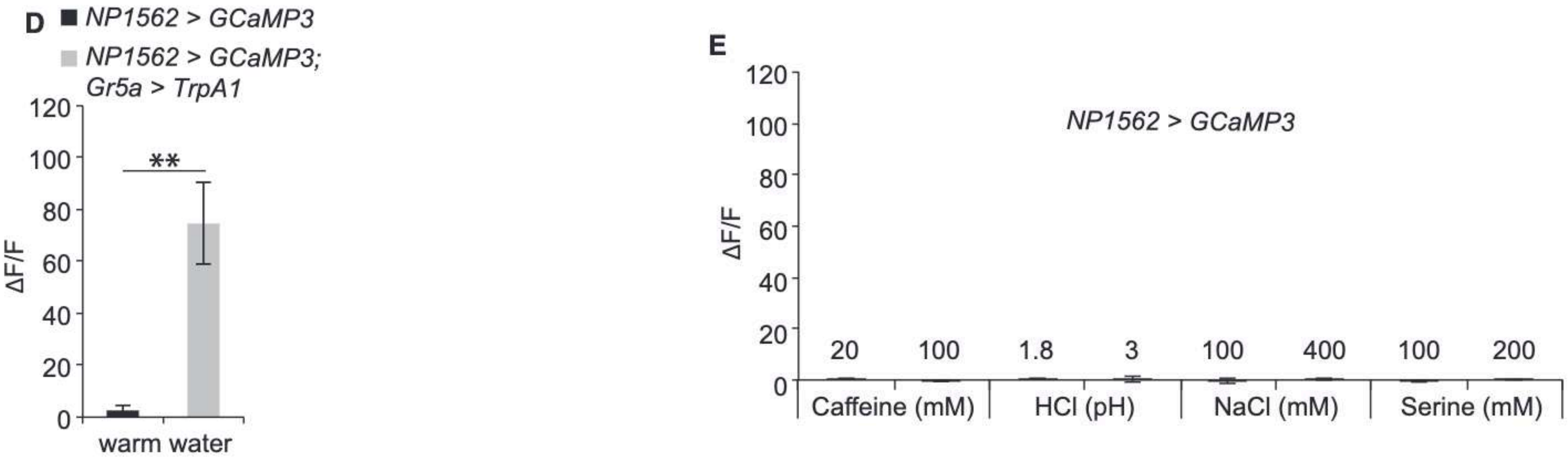


NP1562 neurons convey information from the SOG to the AMMC

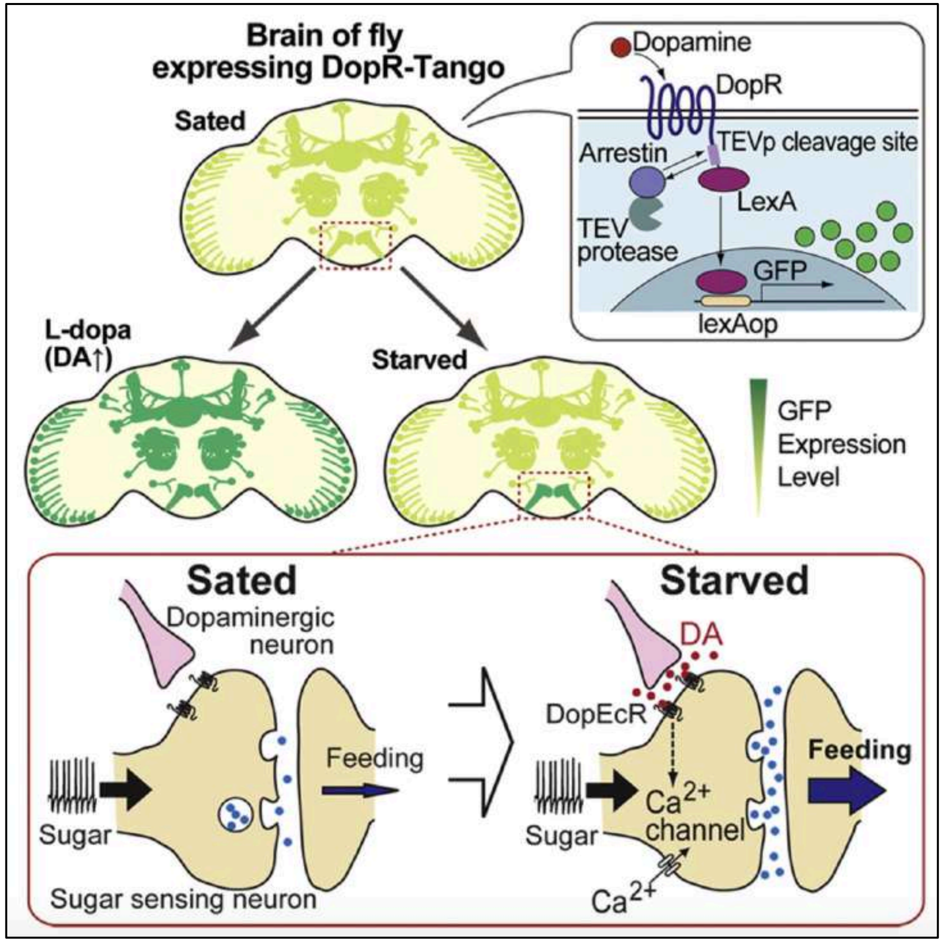
NP1562 sGPNs neurons are activated by sucrose (Sucrose was applied to the proboscis).



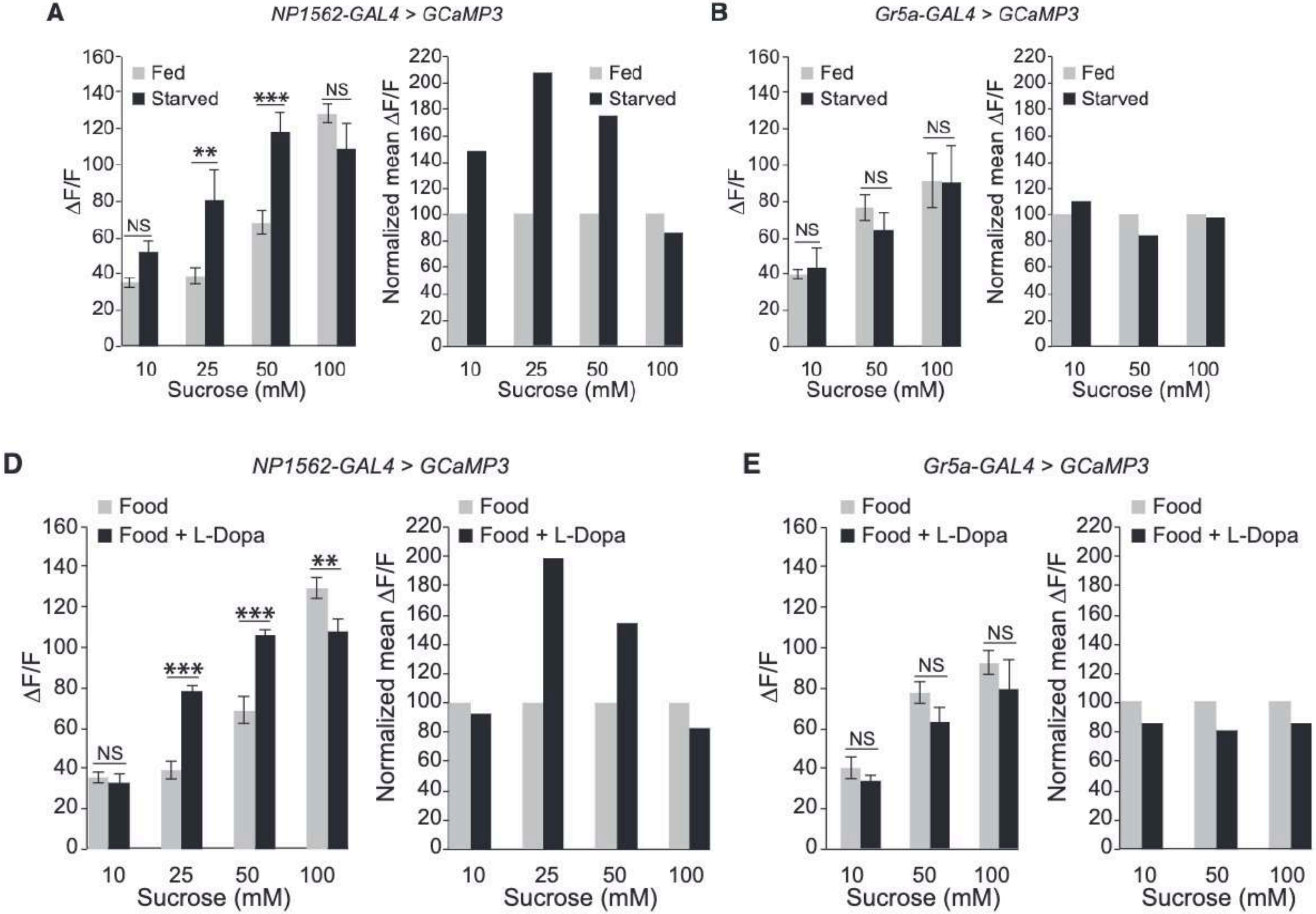
NP1562 sGPNs are functionally connected to Gr5a+ sweet taste neurons and dedicated to processing sweet taste.



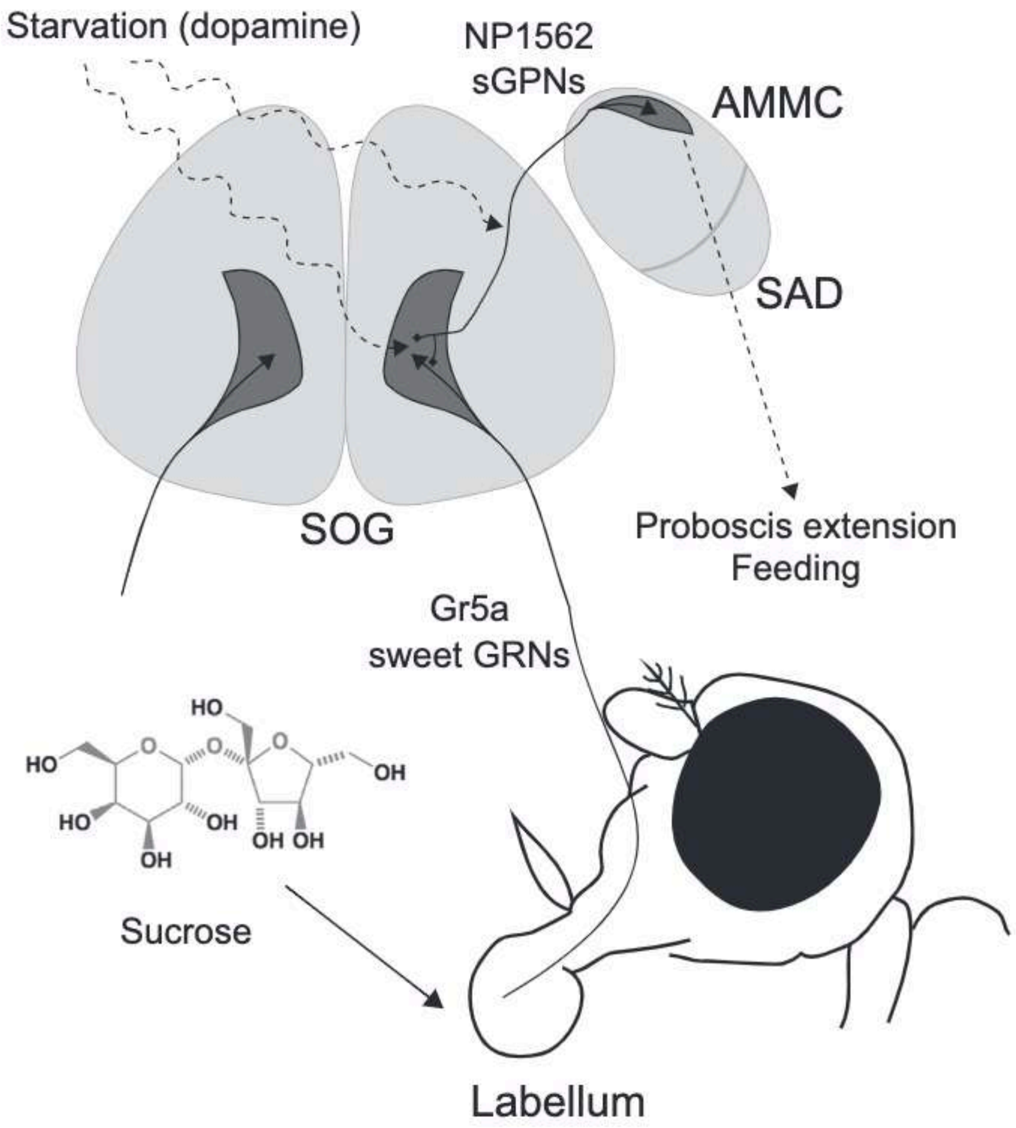
Hunger enhance behavioral sensitivity to sugar by the release of dopamine onto primary gustatory sensory neurons.



Starvation increases the sucrose sensitivity of NP1562



Inagaki, H. K. et al.. Cell 148, 583–595 (2012).


Starvation (dopamine)
NP1562
sGPNs
AMMC
SAD
SOG
Proboscis extension
Feeding
Gr5a
sweet GRNs
HO
O
OH
Sucrose
Labellum

eLIFE
elifesciences.org

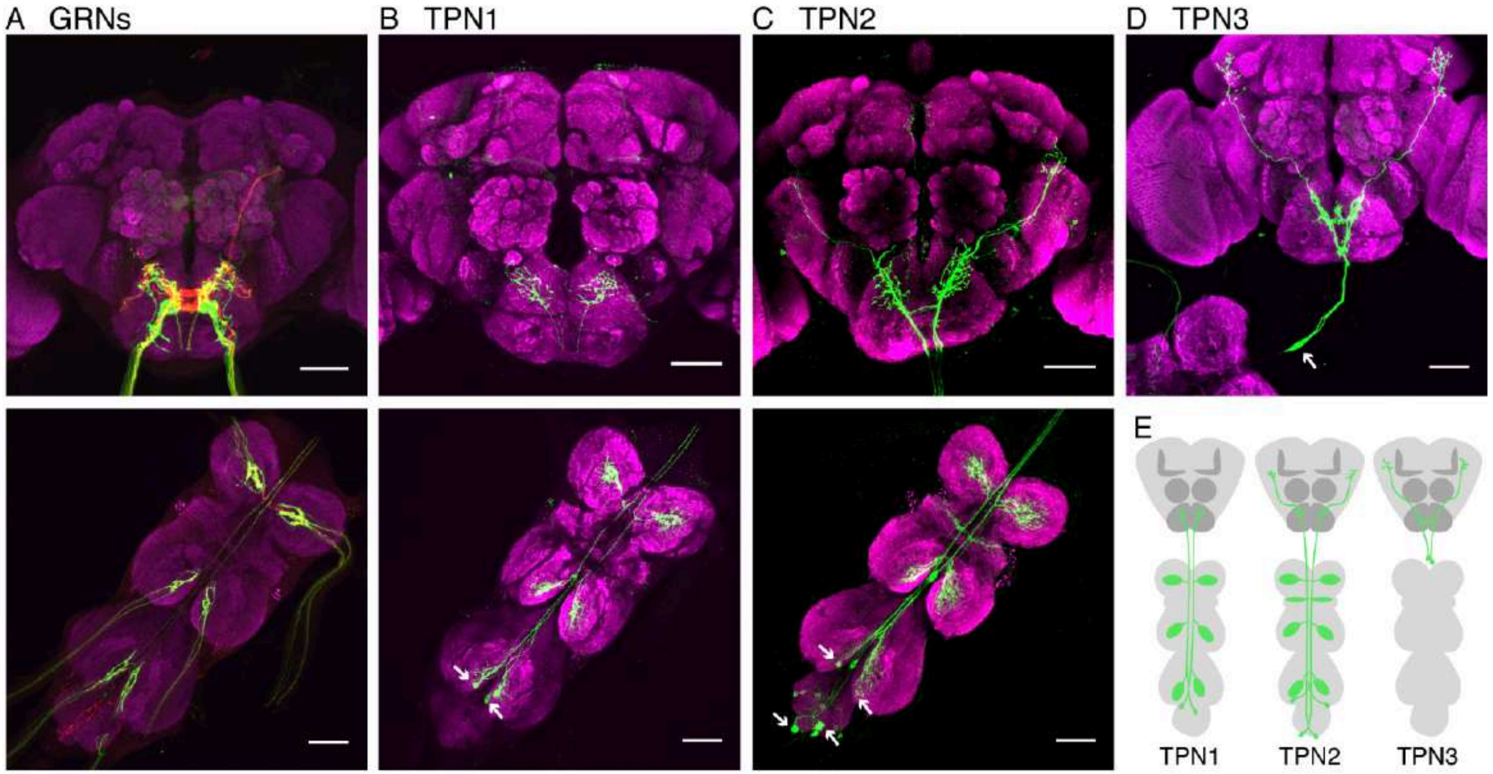
RESEARCH ARTICLE

Long-range projection neurons in the taste circuit of *Drosophila*

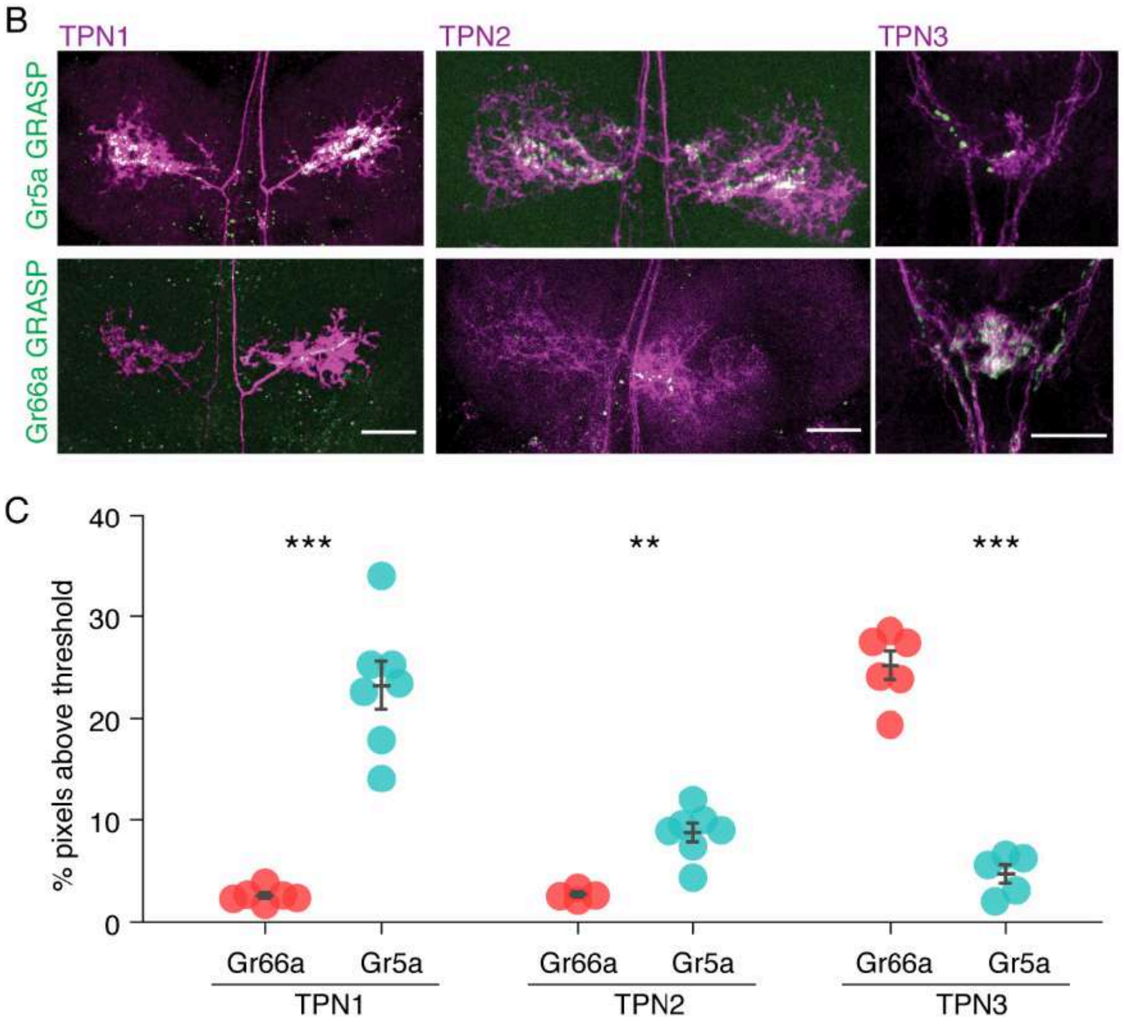
Heesoo Kim[1,2]*, Colleen Kirkhart[1,2], Kristin Scott[1,2]*

[1]Department of Molecular and Cell Biology, University of California, Berkeley, Berkeley, United States; [2]Helen Wills Neuroscience Institute, University of California, Berkeley, Berkeley, United States

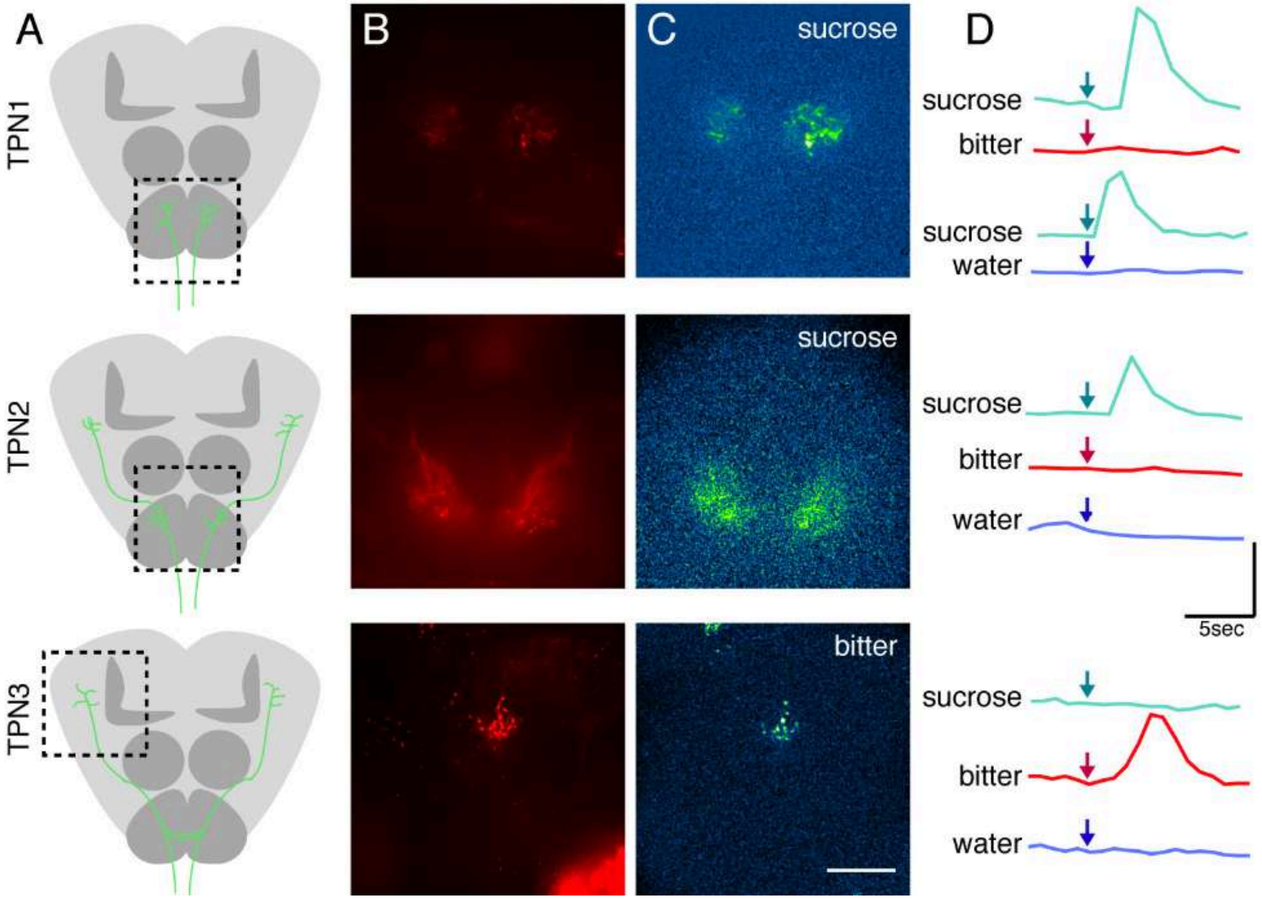
"We searched for neurons in a visual screen of more than 8000 images of Gal4 lines from existing collections."



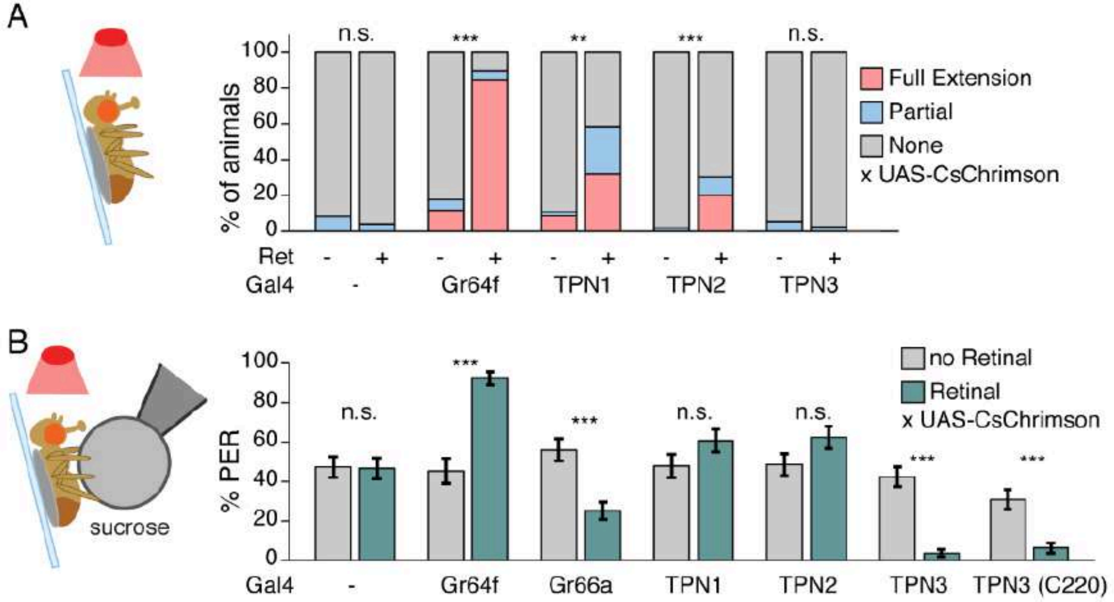
TPNs are in close proximity to gustatory projections.



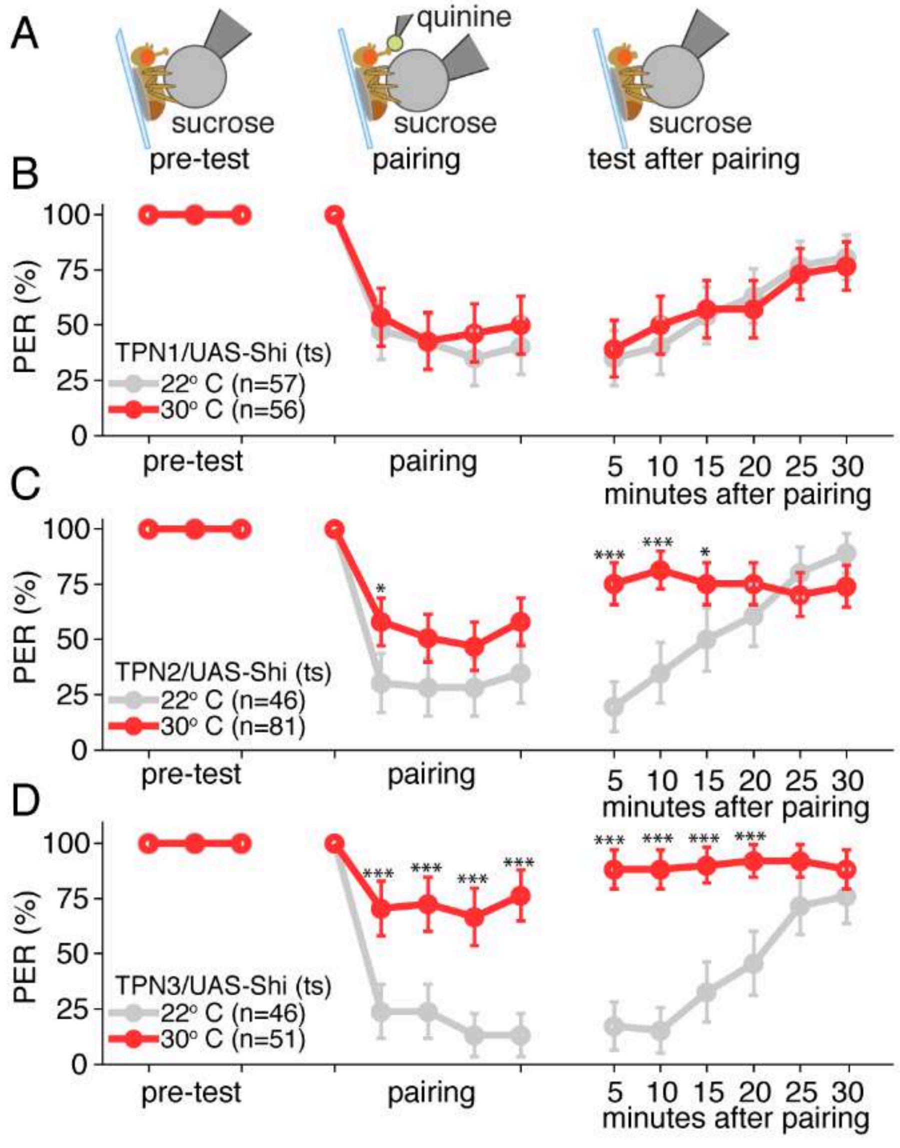
TPNs respond to taste compounds.



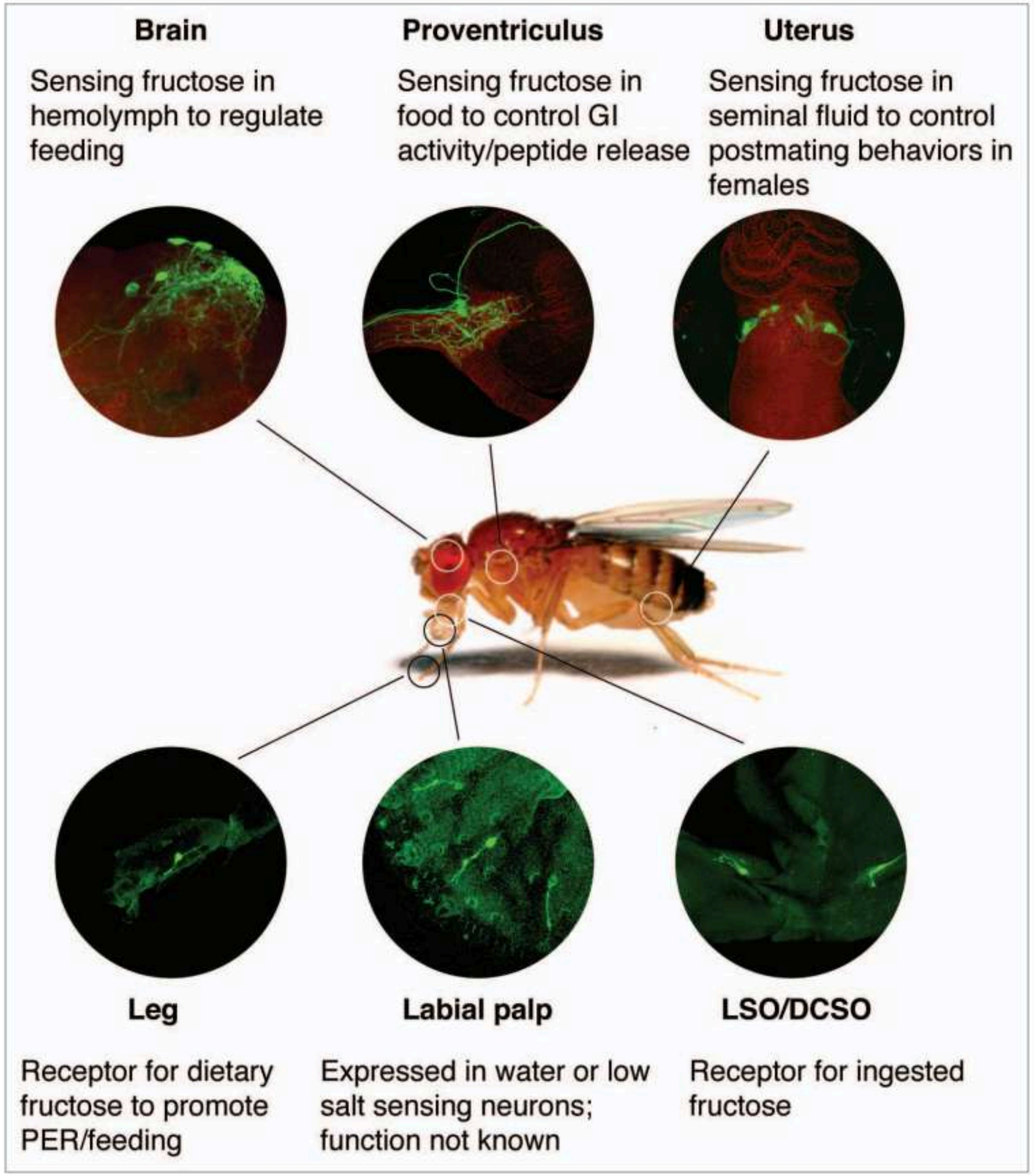
Taste projection neurons influence proboscis extension.



Taste projection neurons are essential for conditioned taste aversion.



Diverse roles for the Drosophila fructose sensor Gr43a



A Fructose Receptor Functions as a Nutrient Sensor in the *Drosophila* Brain

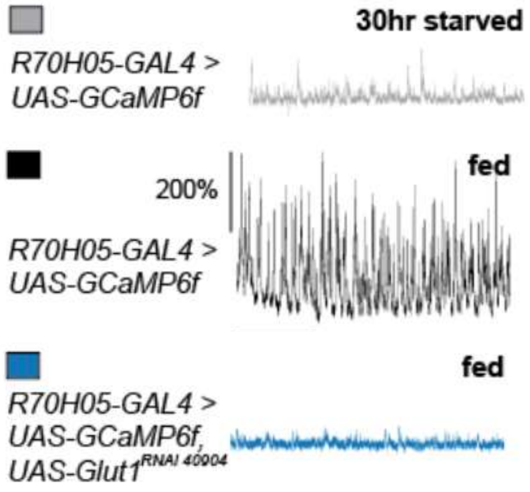
Cell

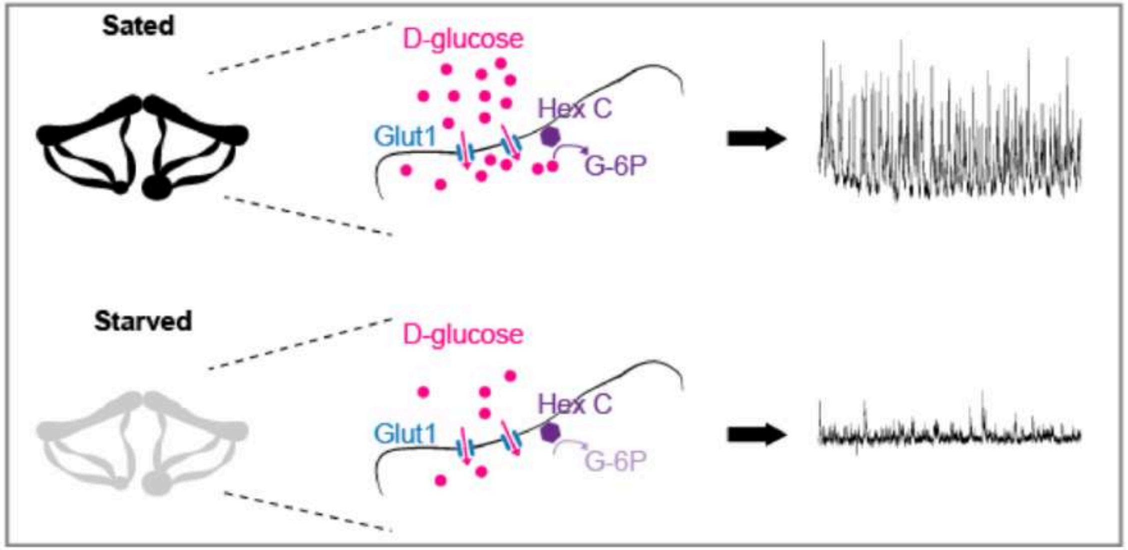
Tetsuya Miyamoto,[1] Jesse Slone,[1,2] Xiangyu Song,[1,3] and Hubert Amrein[1,*]
[1]Department of Molecular and Cellular Medicine, Texas A&M Health Science Center, College Station, TX 77845, USA
[2]Present address: Department of Biological Sciences, Vanderbilt University, Nashville, TN 37235, USA
[3]Present address: Procter & Gamble Technology (Beijing), 35 Yu'an Road, Shunyi District, Beijing, PR China, 101312
Dedicated to the memory of Isabel Sofia Sitcheran Amrein
*Correspondence: amrein@tamhsc.edu
http://dx.doi.org/10.1016/j.cell.2012.10.024

A neural circuit linking two sugar sensors regulates satiety-dependent fructose drive in *Drosophila*.

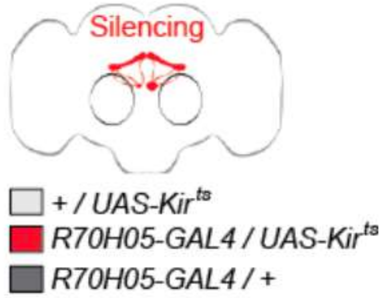
Pierre-Yves Musso[1], Pierre Junca[1], and Michael D Gordon[1,2*]
[1]University of British Columbia, Canada
[2]Lead contact
*Correspondence: gordon@zoology.ubc.ca

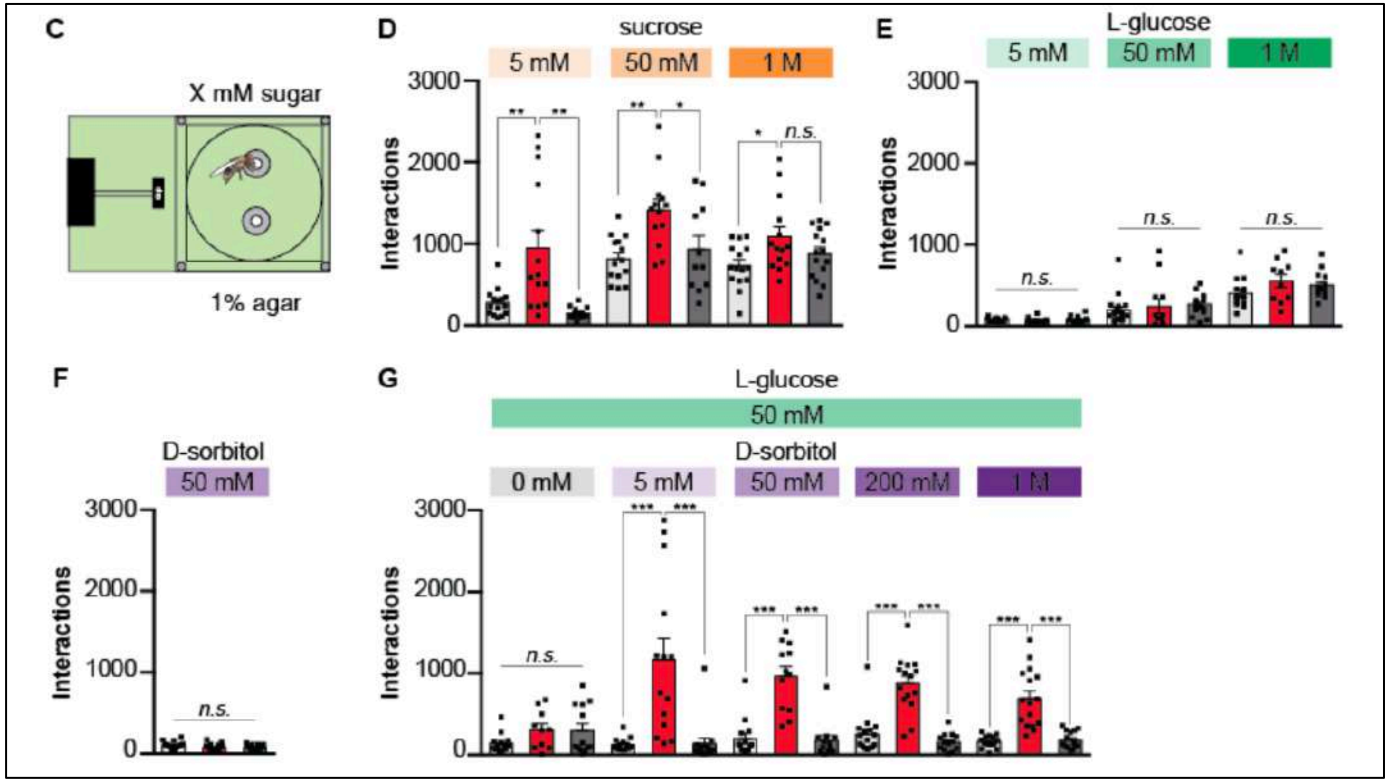
Starvation regulates Fan-Shaped Body oscillations

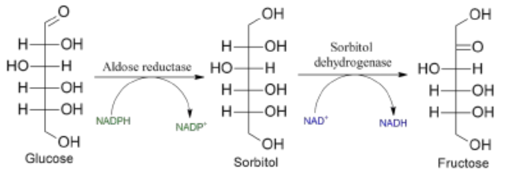


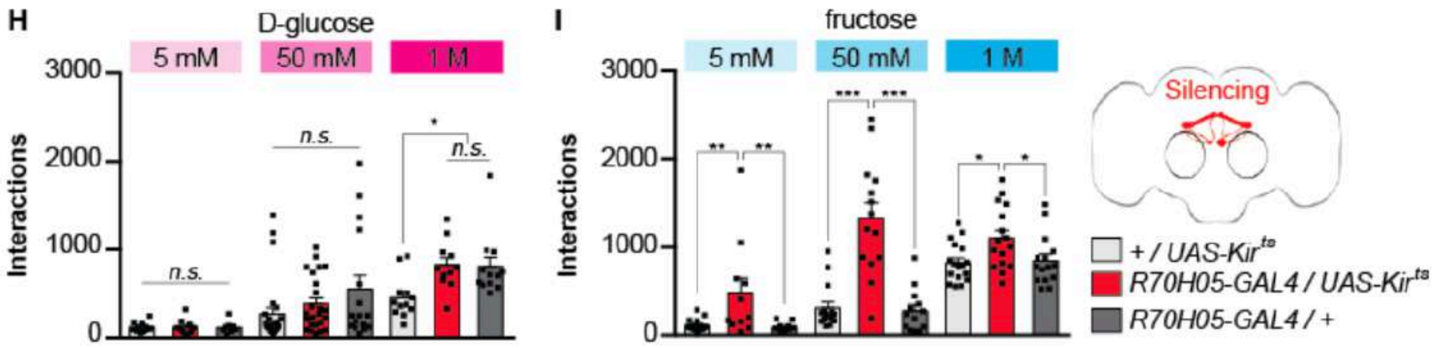


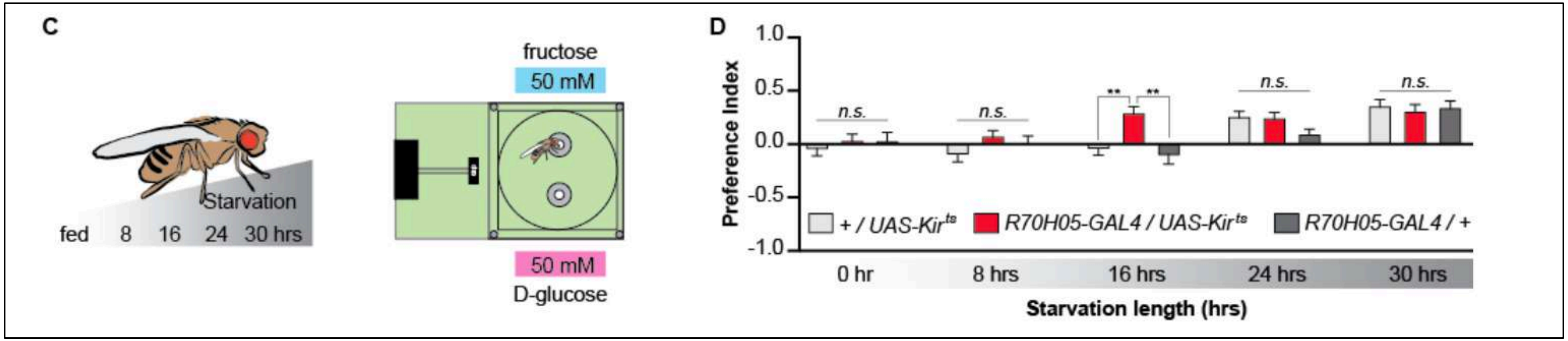
Silencing AB-FB18 neurons increases fructose feeding



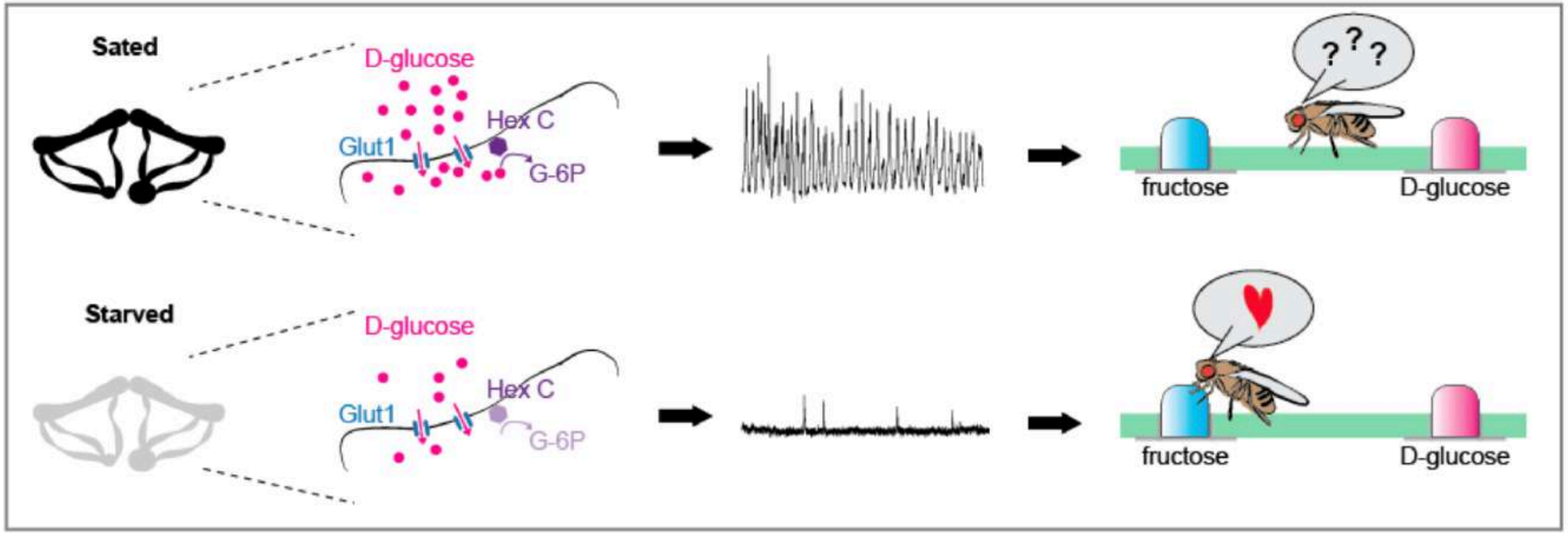




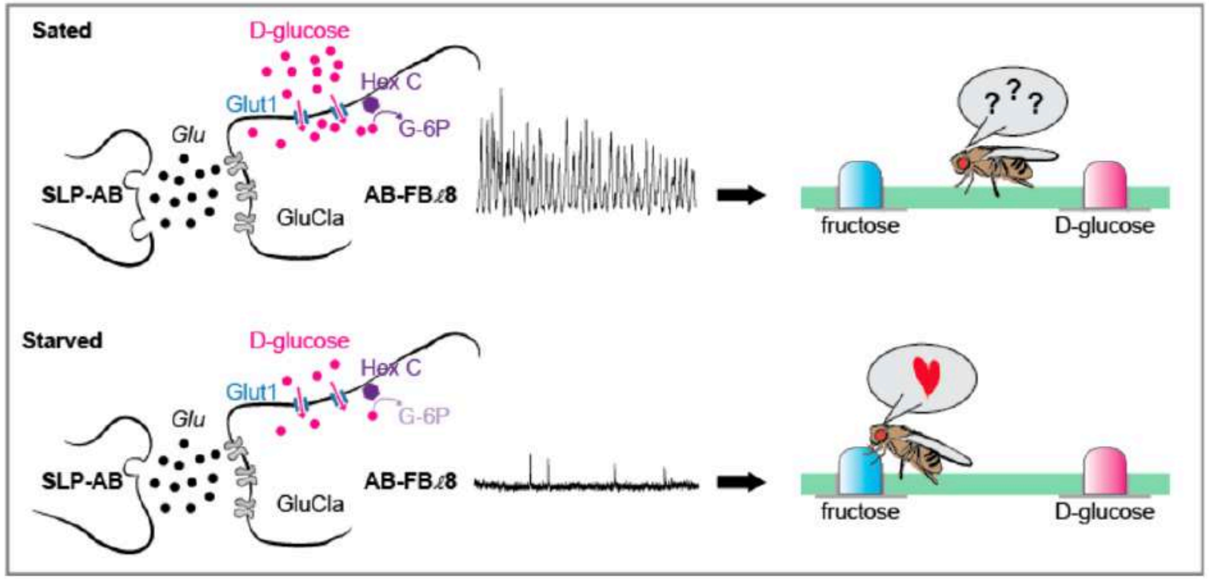




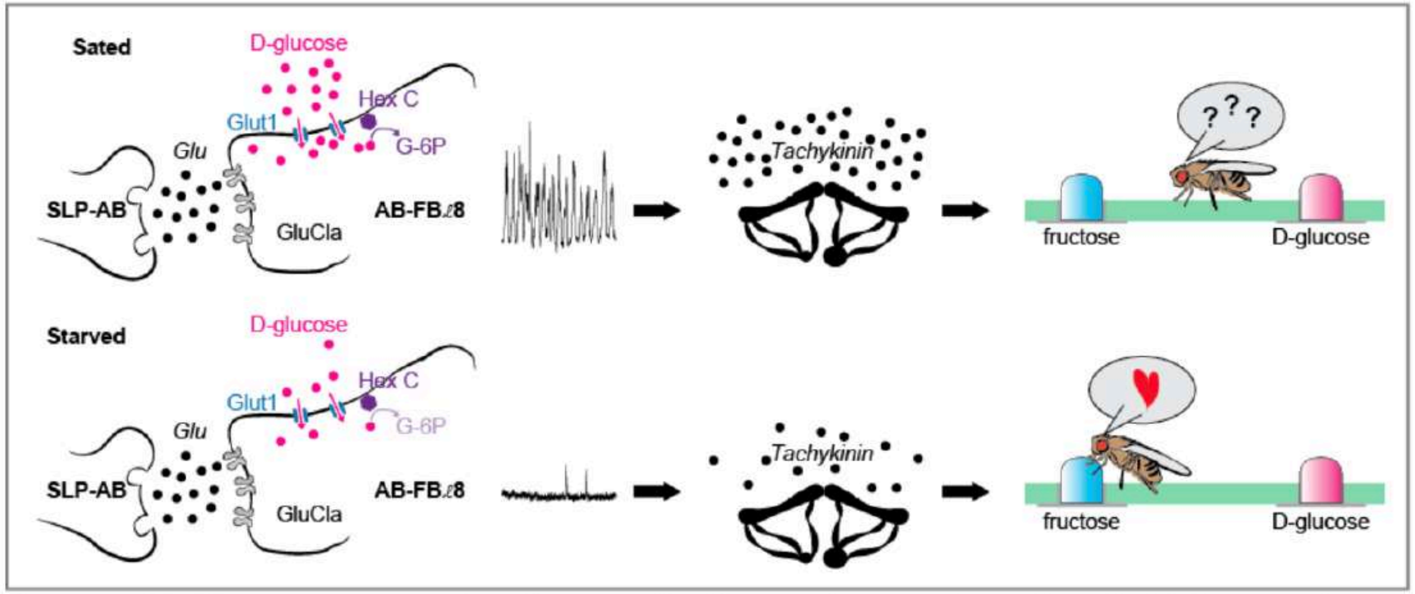
Fructose feeding preference relies on starvation



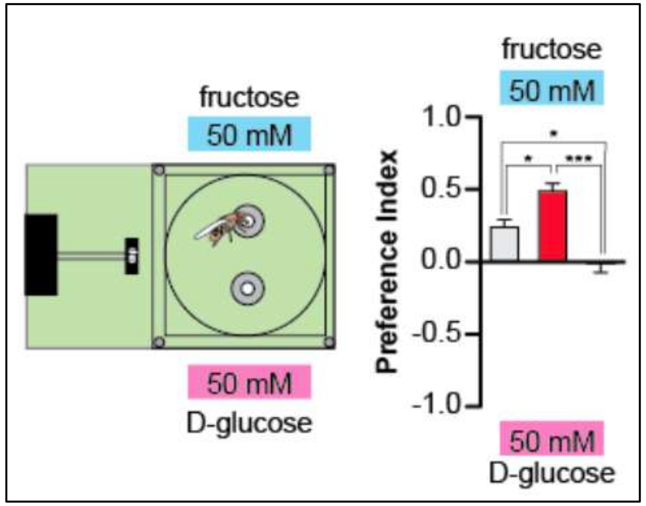
SLP-AB impact behavior by promoting AB-FBl8 oscillations via the action of glutamate on GluCla

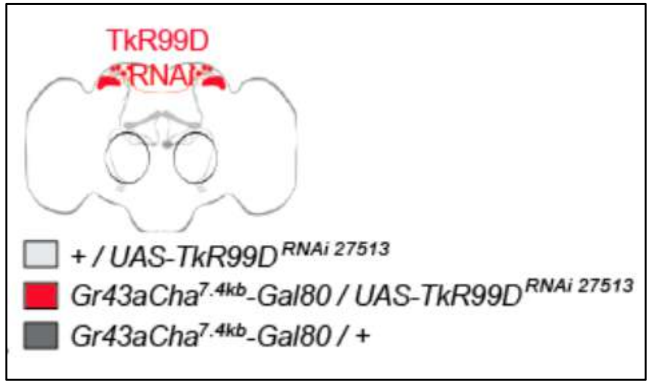


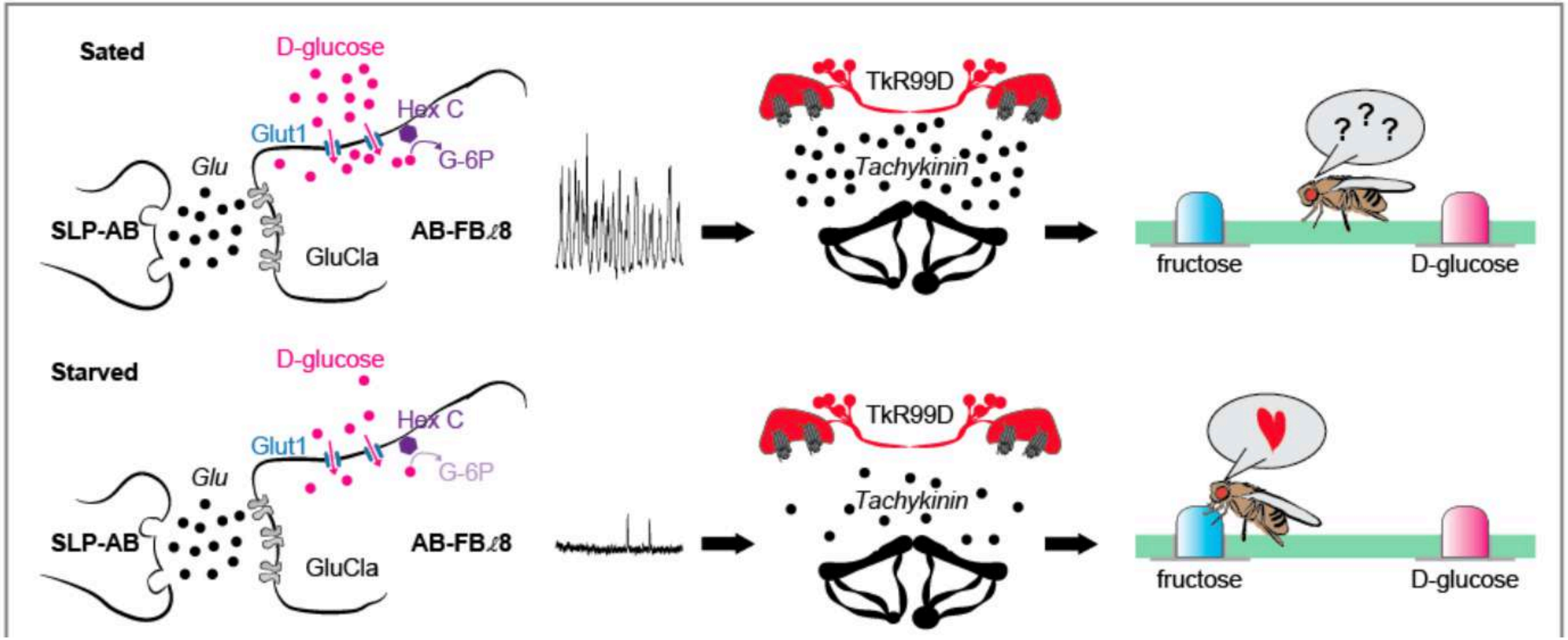
AB-FBl8 neurons regulate fructose-feeding preference through tachykinin secretion

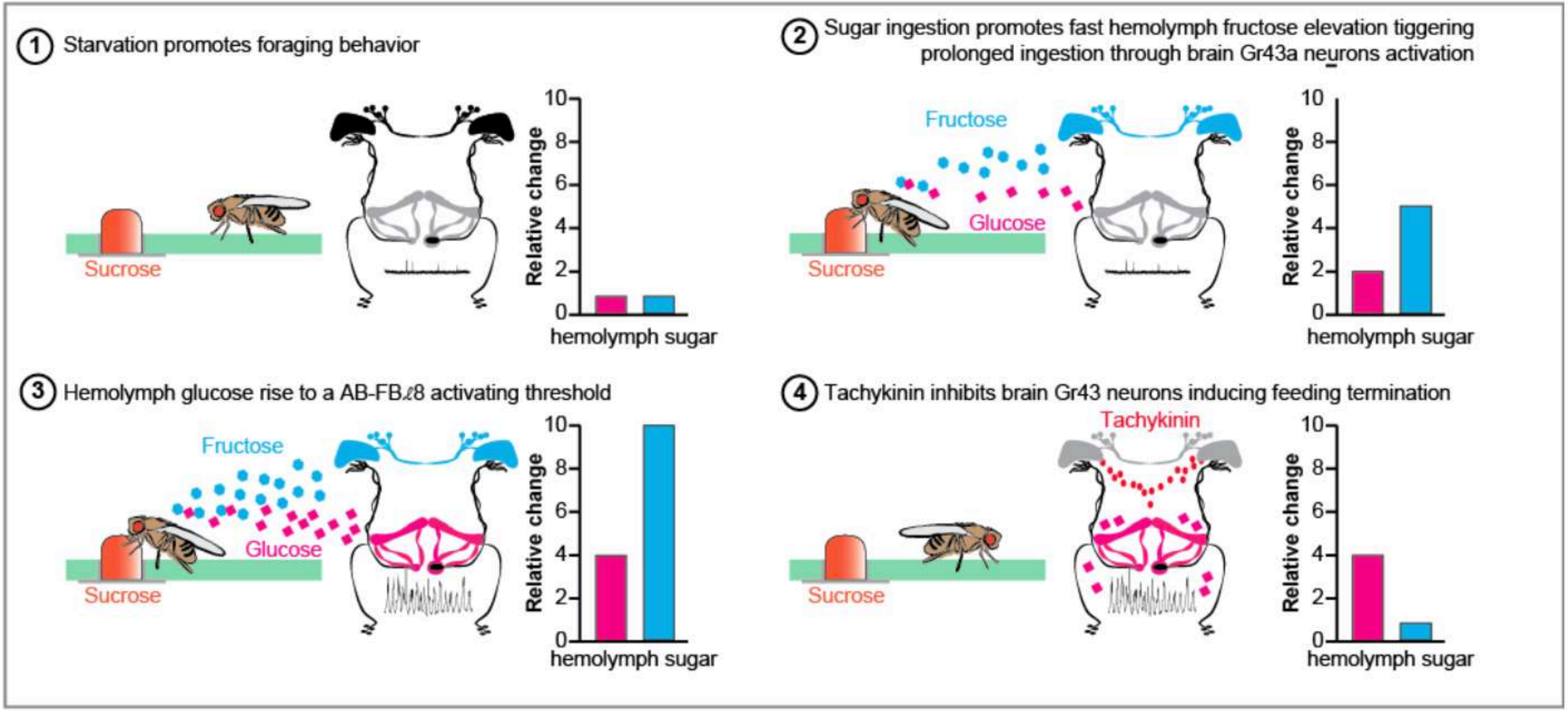


AB-FBl8 regulates fructose feeding via tachykinin signalling to Gr43a neurons.









1 Starvation promotes foraging behavior
Sucrose
10
8
6
4
2
0
Relative change
hemolymph sugar
2 Sugar ingestion promotes fast hemolymph fructose elevation tiggering prolonged ingestion through brain Gr43a neurons activation
Fructose
Glucose
Sucrose
Relative change
hemolymph sugar
3 Hemolymph glucose rise to a AB-FBℓ8 activating threshold
Fructose
Glucose
Sucrose
Relative change
hemolymph sugar
4 Tachykinin inhibits brain Gr43 neurons inducing feeding termination
Tachykinin
Sucrose
Relative change
hemolymph sugar

Take-home message

1. SOG is the first relay center of taste processing in the brain

2. Sweet GRNs originating from different organs exhibit distinct axonal projection patterns in the subesophageal zone (SEZ),

3.Input from each taste organ is relayed to distinct higher-order neuronal circuits, which in turn regulate different aspects of feeding behavior.

GRNs(Gr5a+) in legs terminate in VNC: locomotion,

GRNs(Gr64f+,Gr61a+) in legs terminate in SOG: feeding initiation

GRNs in pharynx : maintain ingestion

GRNs in labellum(Gr5a+): proboscis extention

4. Gustatory receptor(Gr43a) also expressed in the brain neurons as a nutrient sensors to control sugar consumption.

THREE.

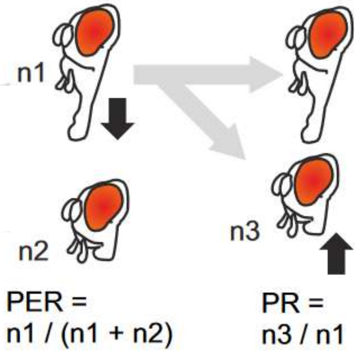
The Integration of Sweet Taste And Other Information

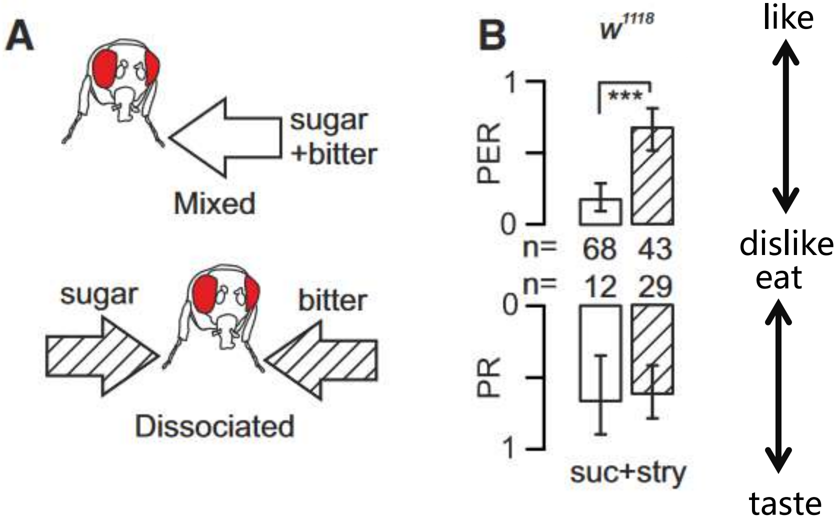
MMZ

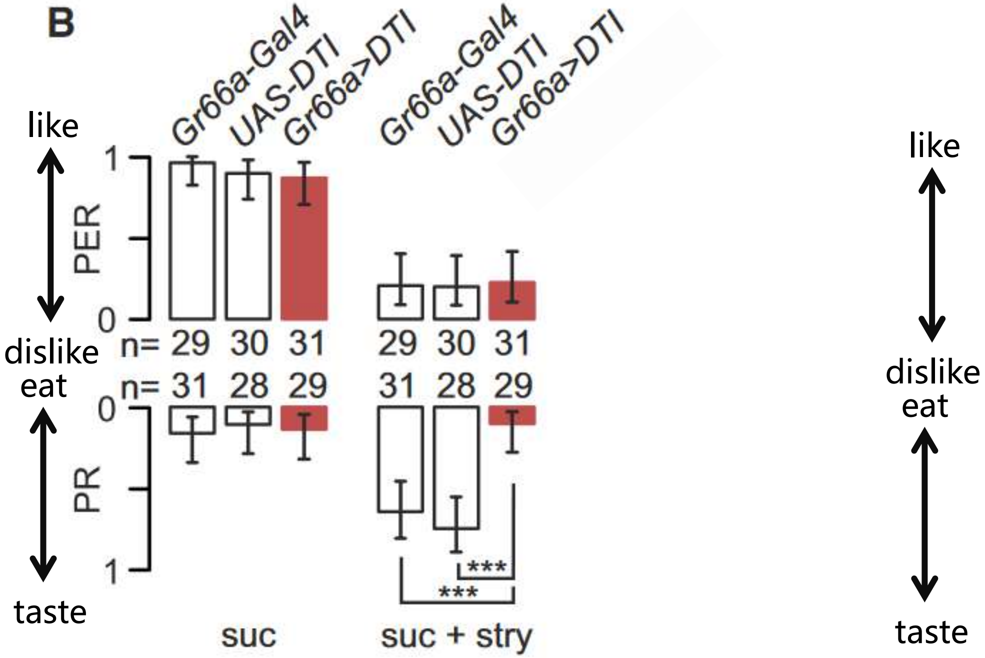
The integration of sweet taste and other information

- Signal integration in taste sensilla
- Other signal with sweet taste influence behavior

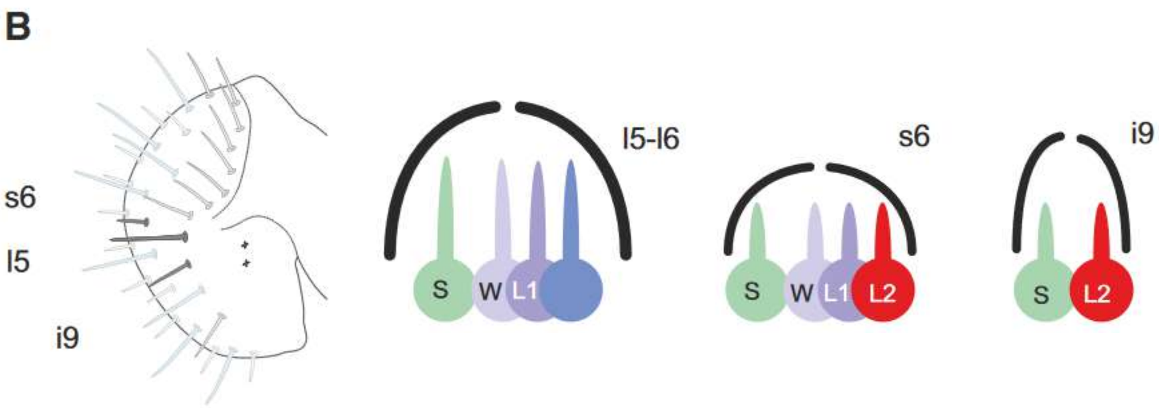
Sweet plus bitter, eat or not

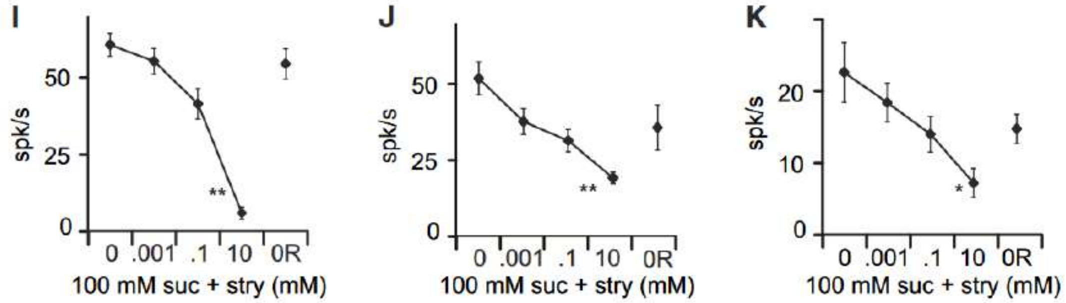


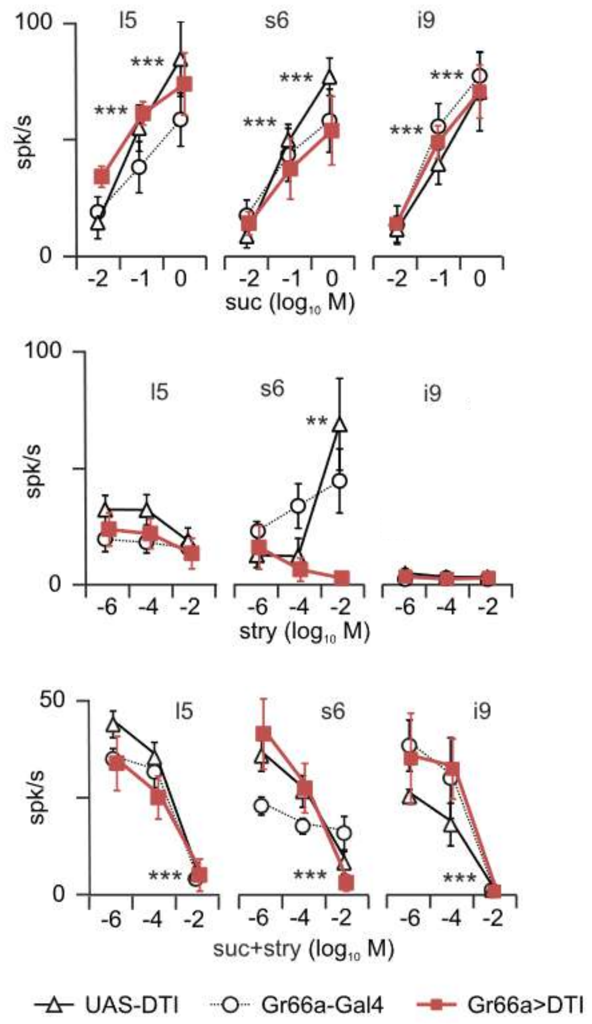




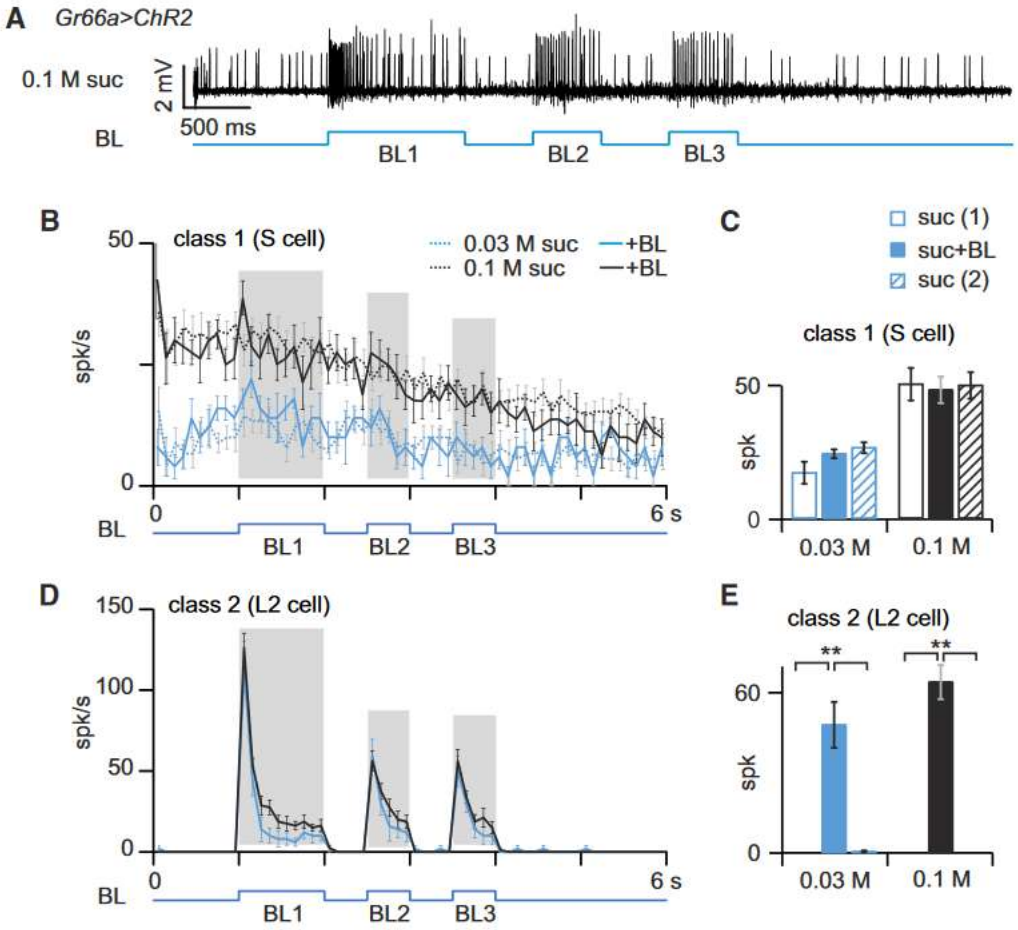
Bitter-neurons are unnecessary for inhibiting sweet perception

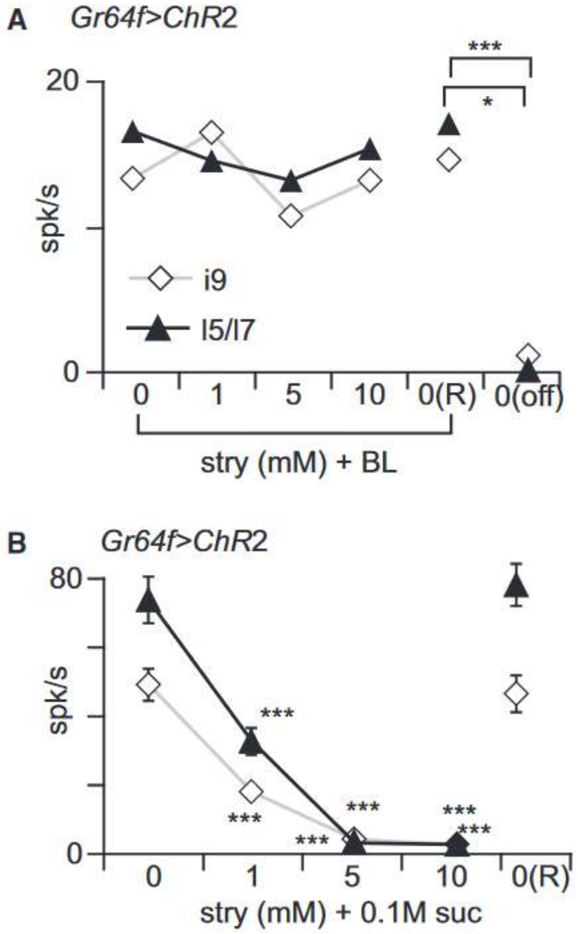




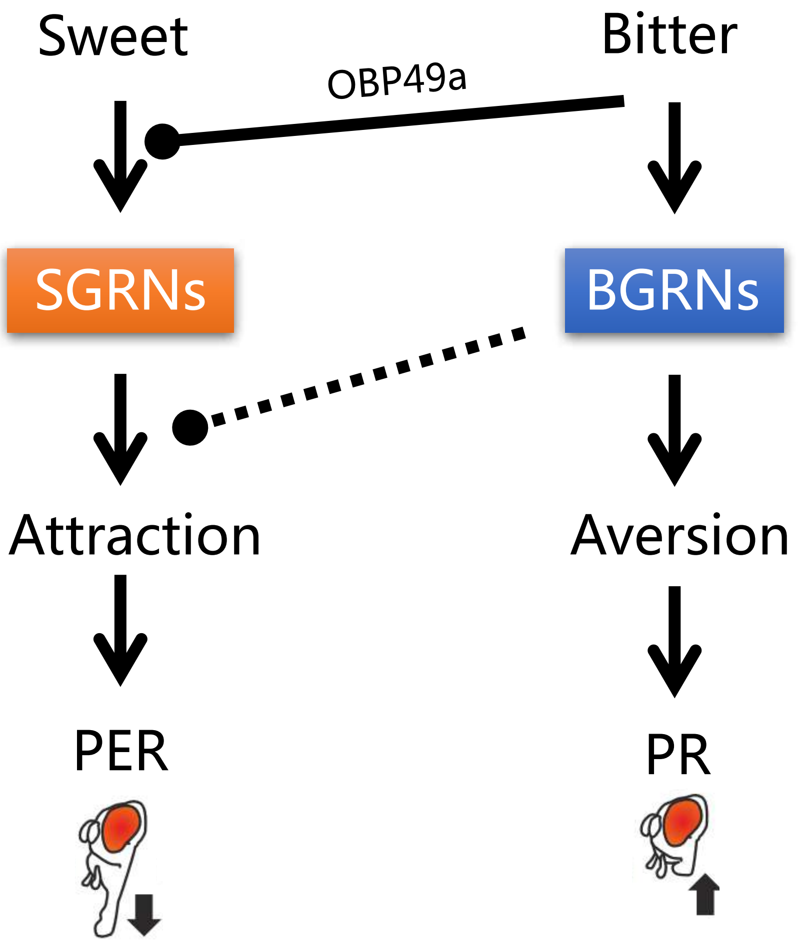


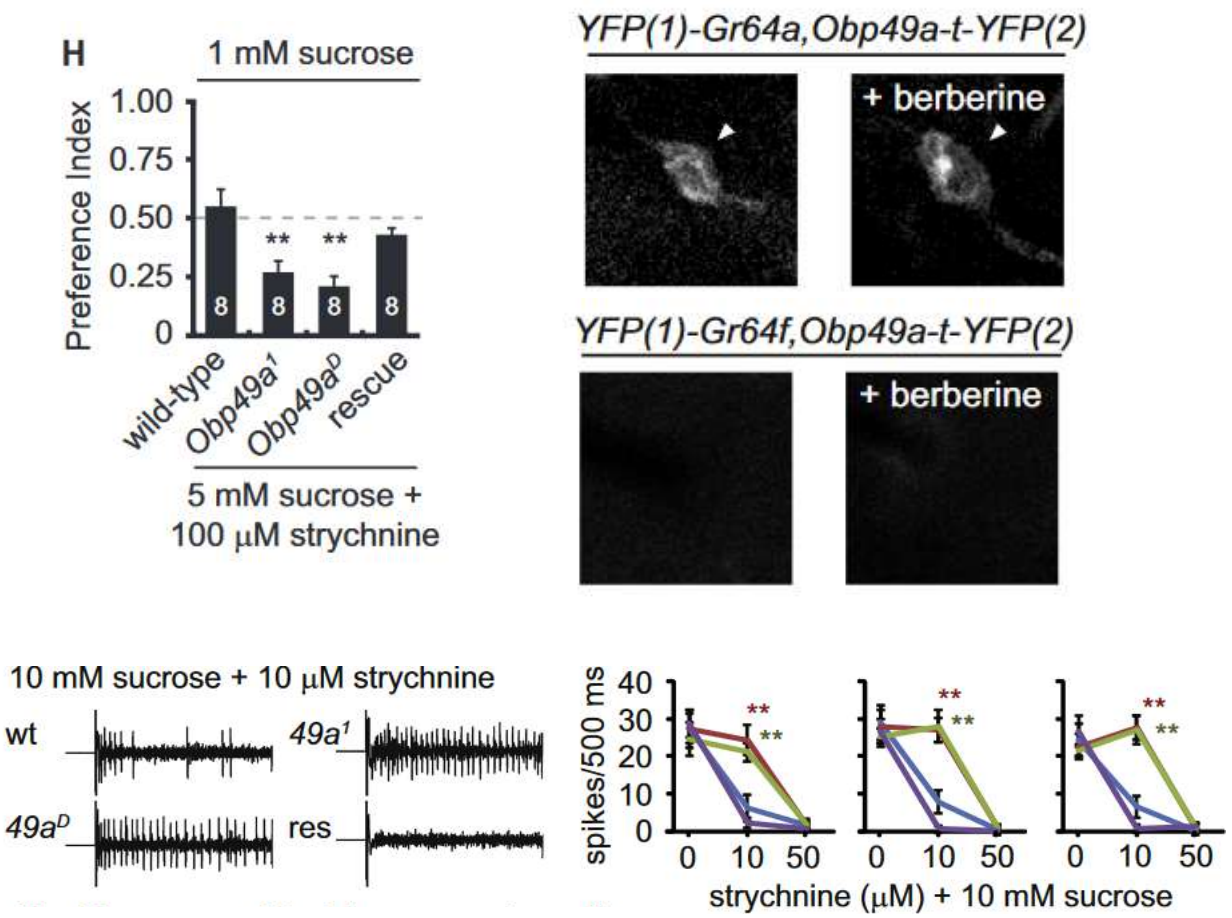
Activation of bitter neurons does not affect the activity of sweet neurons

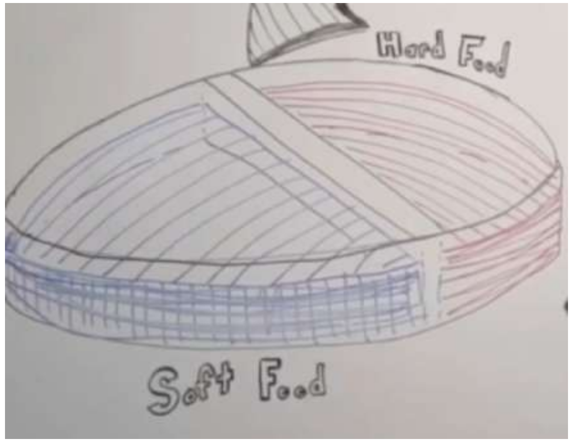




Summary1


Sweet
Bitter
OBP49a
SGRNs
BGRNs
Attraction
Aversion
PER
PR


H
1 mM sucrose
Preference Index
1.00
0.75
0.50
0.25
0
**
**
8
8
8
8
wild-type
Obp49a1
Obp49aD
rescue
5 mM sucrose +
100 μM strychnine
YFP(1)-Gr64a,Obp49a-t-YFP(2)
+ berberine
YFP(1)-Gr64f,Obp49a-t-YFP(2)
+ berberine
10 mM sucrose + 10 μM strychnine
wt
49a1
49aD
res
spikes/500 ms
40
30
20
10
0
**
**
0 10 50
0 10 50
0 10 50
strychnine (μM) + 10 mM sucrose



ARTICLE

Received 3 Feb 2016 | Accepted 10 Aug 2016 | Published 19 Sep 2016 DOI: 10.1038/ncomms12872 OPEN

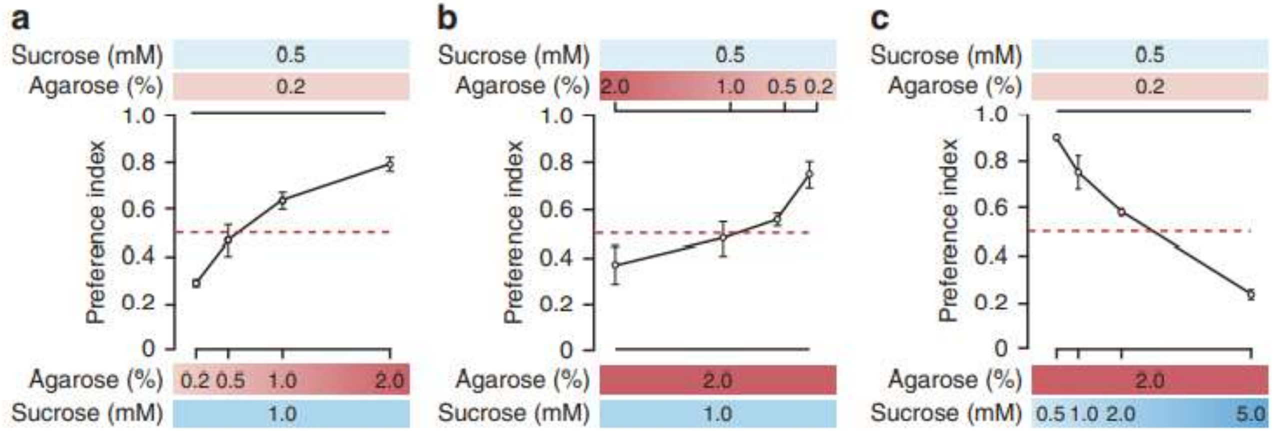
Mechanosensory neurons control sweet sensing in *Drosophila*

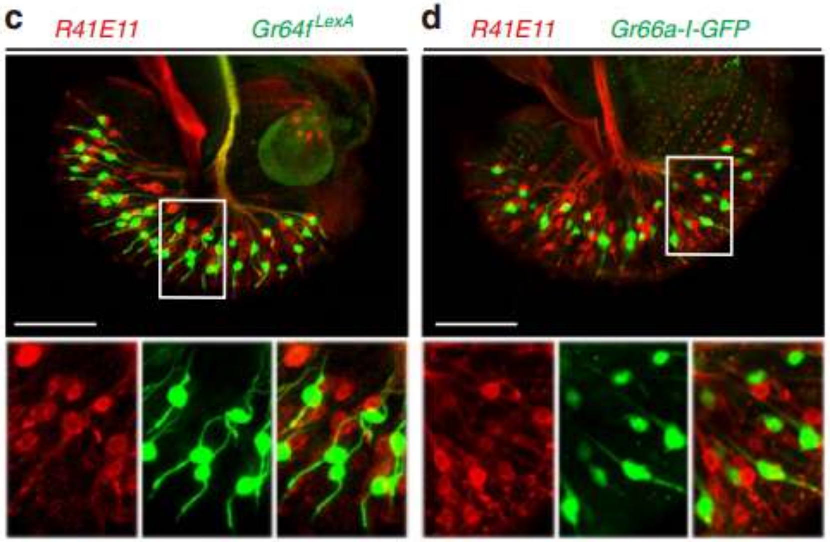
Yong Taek Jeong[1], Soo Min Oh[1], Jaewon Shim[2], Jeong Taeg Seo[1], Jae Young Kwon[3] & Seok Jun Moon[1]

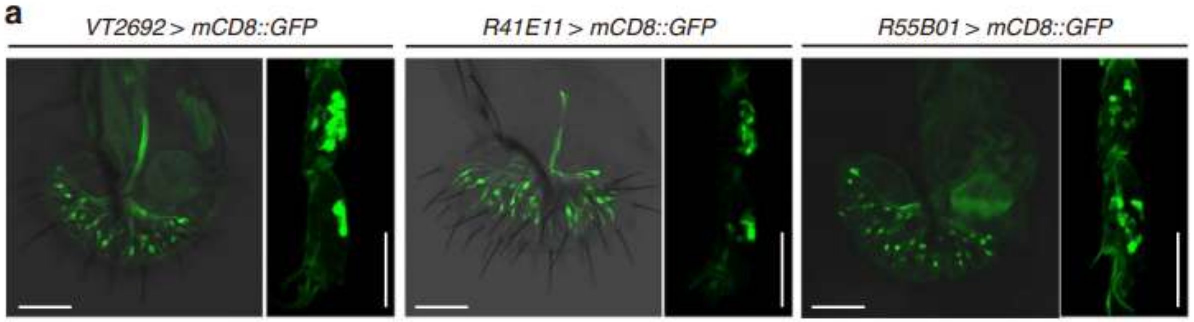
Sweet neurons inhibit texture discrimination by signaling TMC-expressing mechanosensitive neurons in *Drosophila*

Shun-Fan Wu[1,2*], Ya-Long Ja[1], Yi-jie Zhang[1], Chung-Hui Yang[2*]

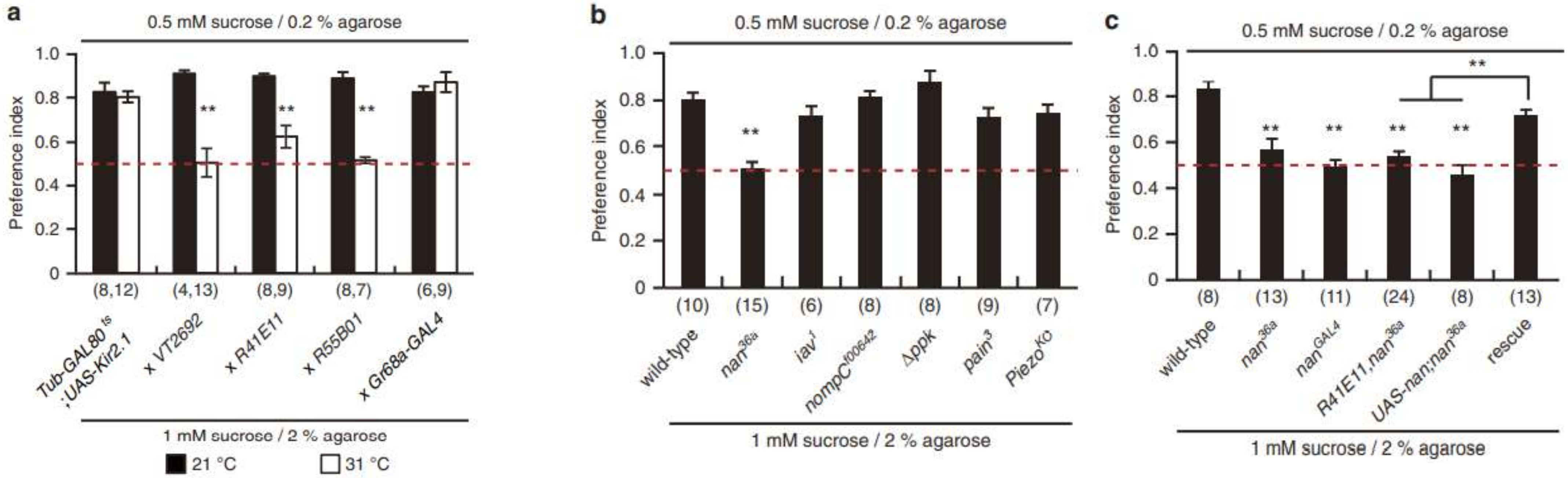
Food hardness affects sugar preference



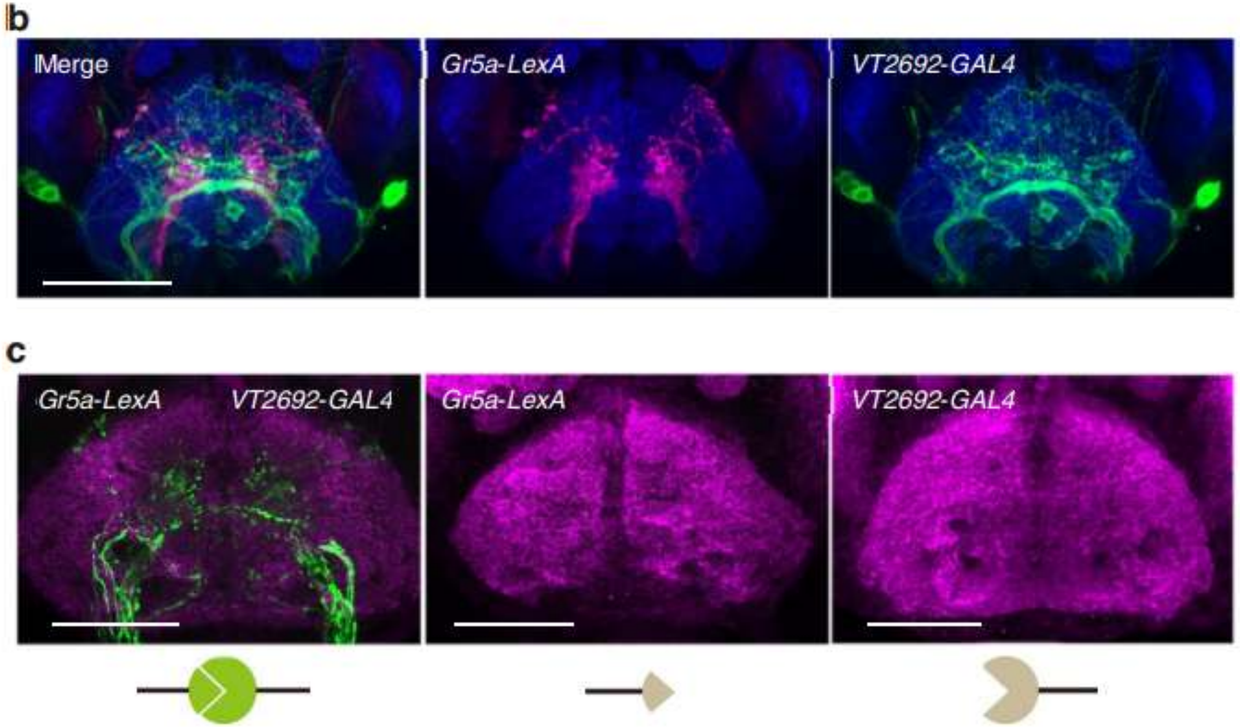


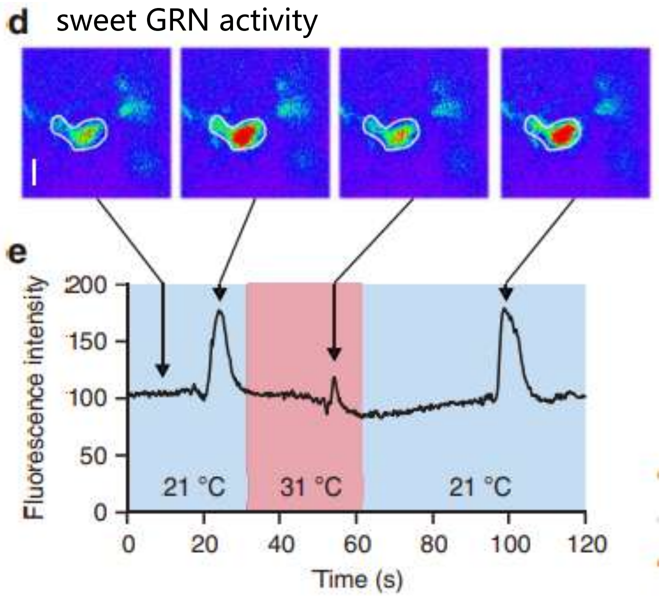


nan in MSN participates in hardness perception

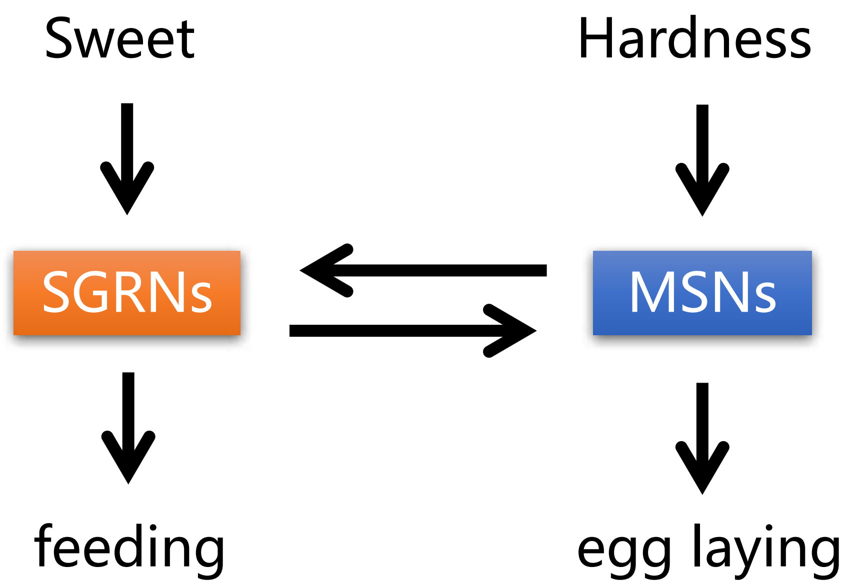


MSNs inhibit sweet GRNs response to sugar





Summary2

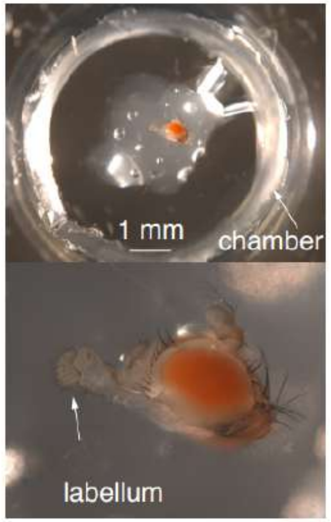


Temperature and sweet taste integration in *Drosophila*

Qiaoran Li[5], Nicolas A. DeBeaubien[5], Takaaki Sokabe[6], Craig Montell[5,*]

GRN cannot respond to low temperatures

E



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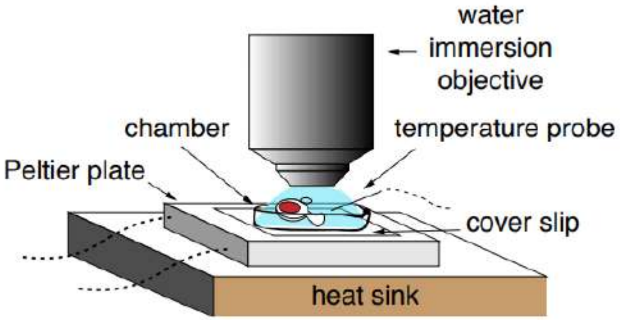
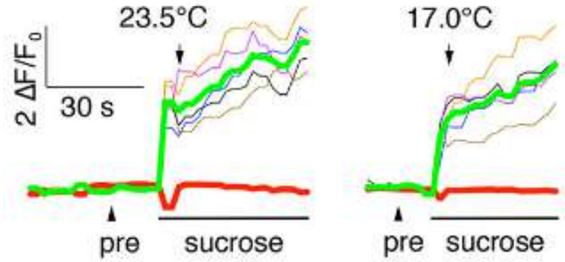
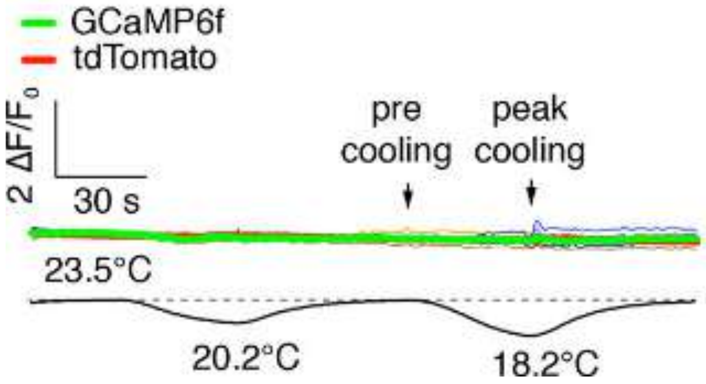
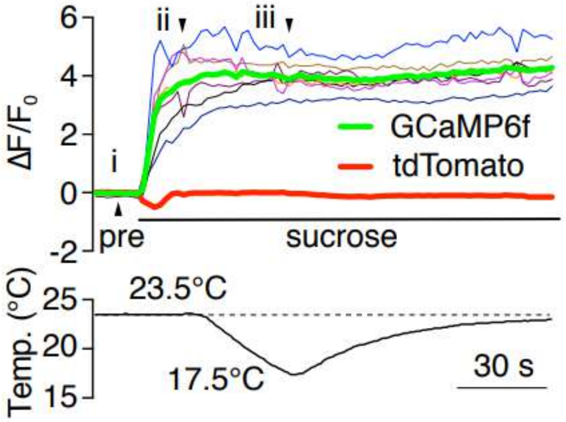
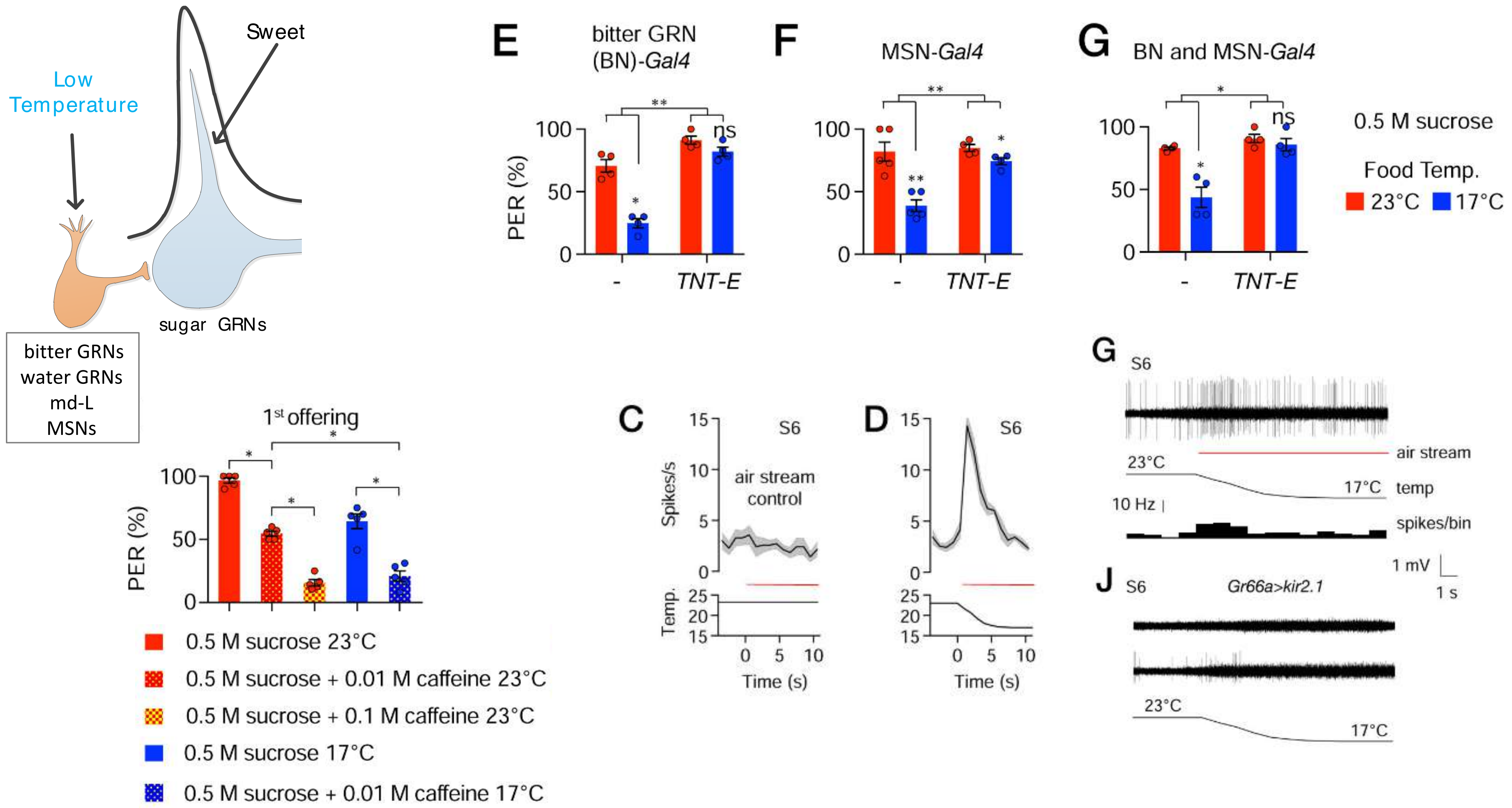




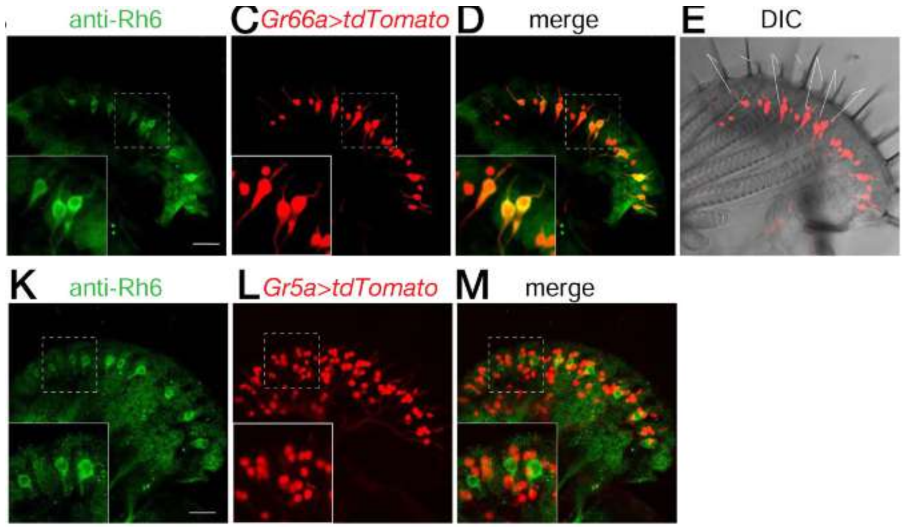


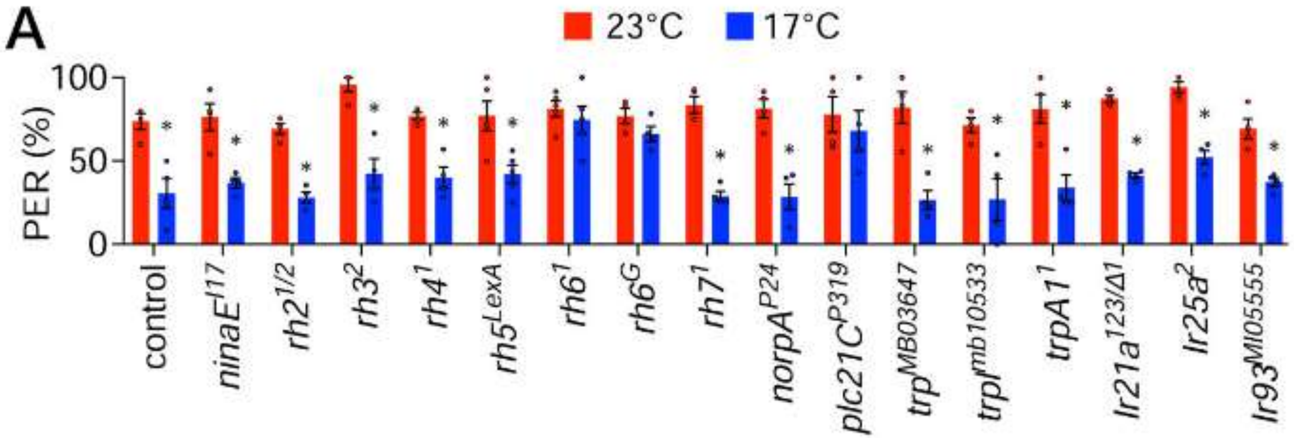


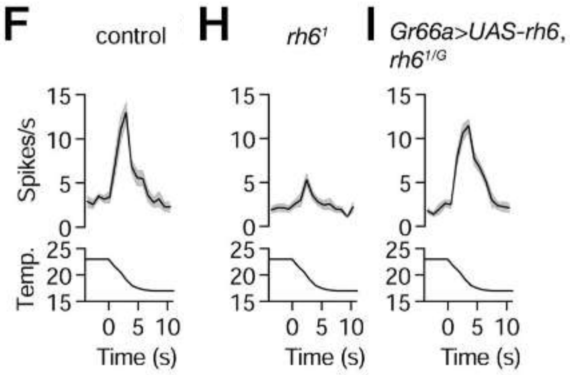
Bitter GRNs and MSNs are required for the cool-induced attenuation of the sugar response

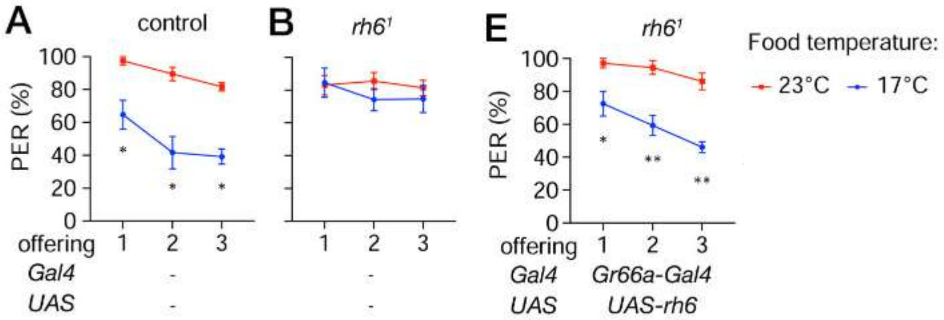


Rh6 is required for activation of bitter GRNs by cooling

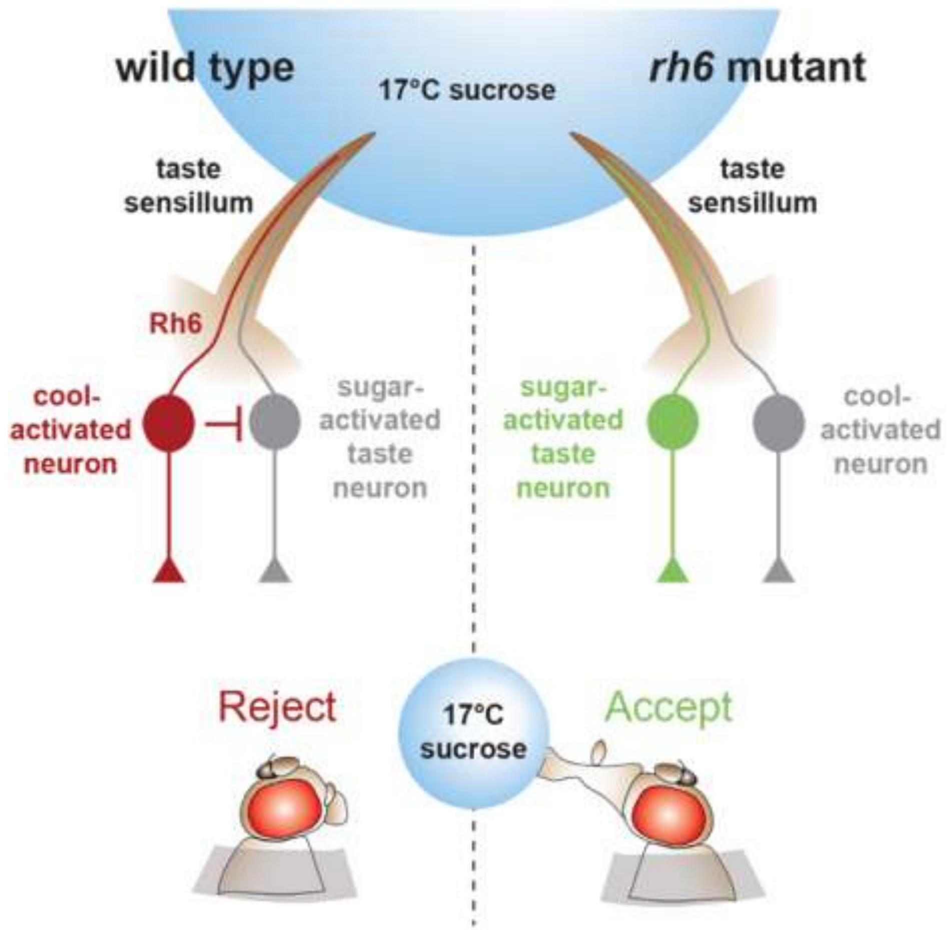








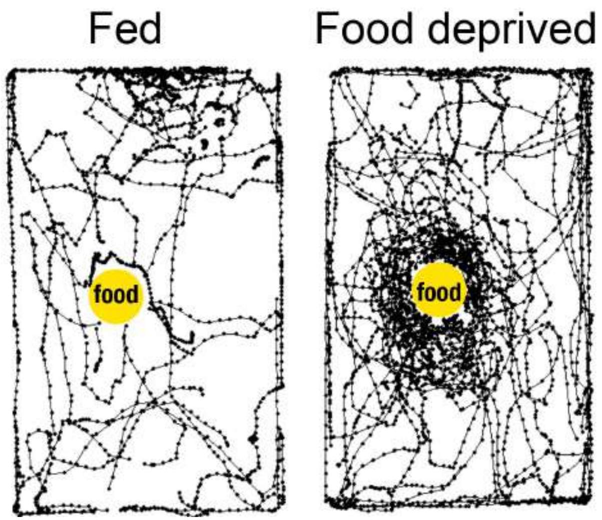
Summary3



wild type
17°C sucrose
rh6 mutant
taste
sensillum
taste
sensillum
Rh6
cool-
activated
neuron
sugar-
activated
taste
neuron
sugar-
activated
taste
neuron
cool-
activated
neuron
Reject
17°C
sucrose
Accept

The integration of sweet taste and other information

- Signal integration in taste sensilla
- Other signal with sweet taste influence behavior



Sweetness induces sleep through gustatory signalling independent of nutritional value in a starved fruit fly

Tatsuya Hasegawa[1], Jun Tomita[1,2], Rina Hashimoto[2], Taro Ueno[2,3], Shoen Kume[2,4] & Kazuhiko Kume[1,2]

Neuron
Volume 84, Issue 4, 19 November 2014, Pages 806-820

CellPress

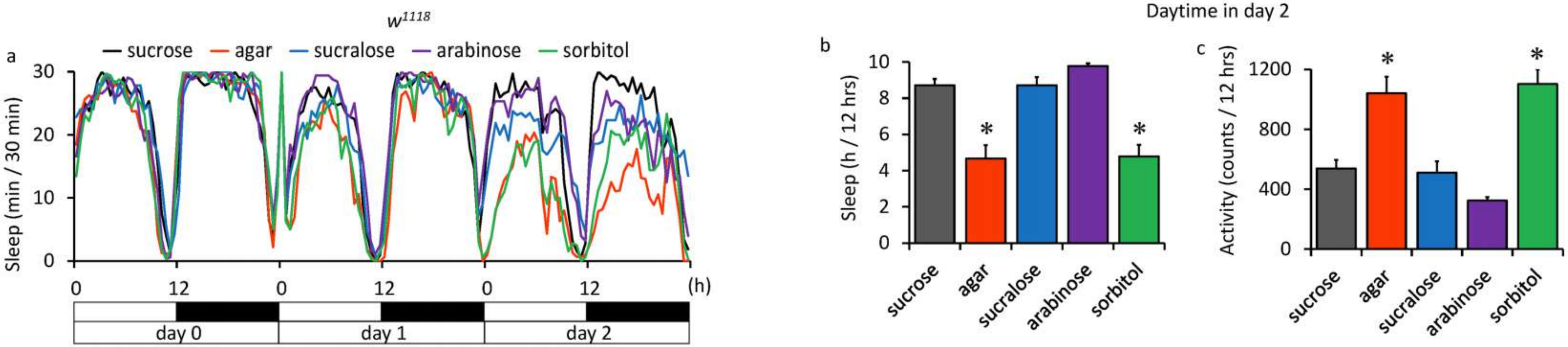
Article

Independent, Reciprocal Neuromodulatory Control of Sweet and Bitter Taste Sensitivity during Starvation in *Drosophila*

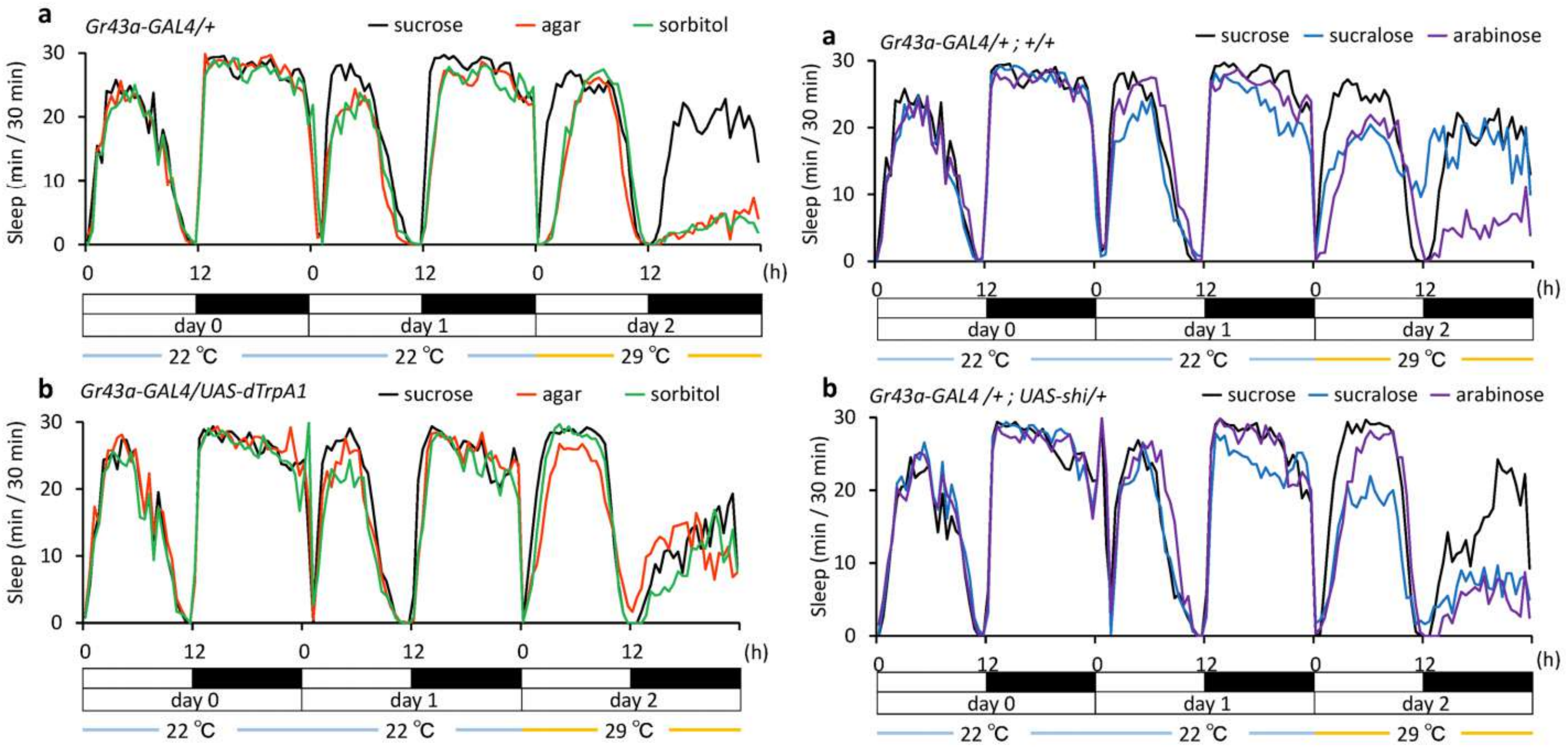
Hidehiko K. Inagaki[1,3], Ketaki M. Panse[1], David J. Anderson[1,2]

Show more

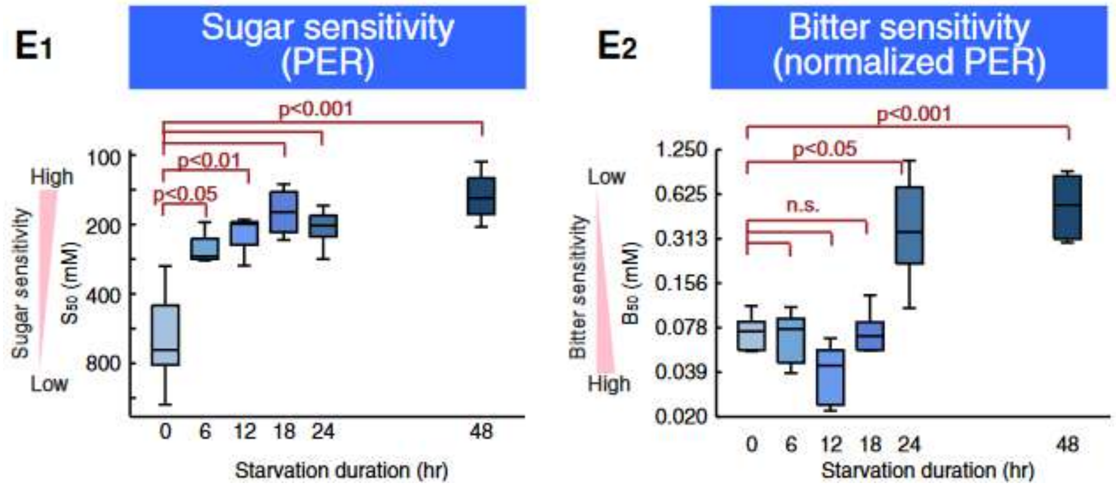
Sweetness promotes sleep in starved flies

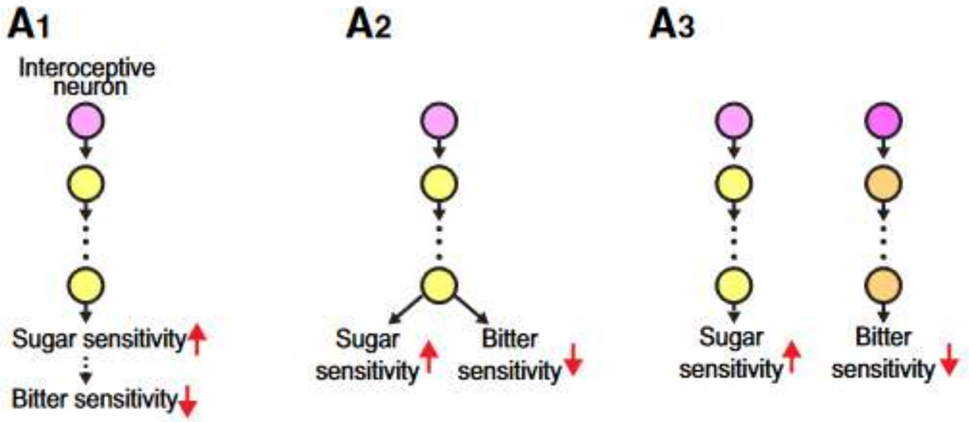


Gr43a neurons is necessary and sufficient for sleep increase of starved flies

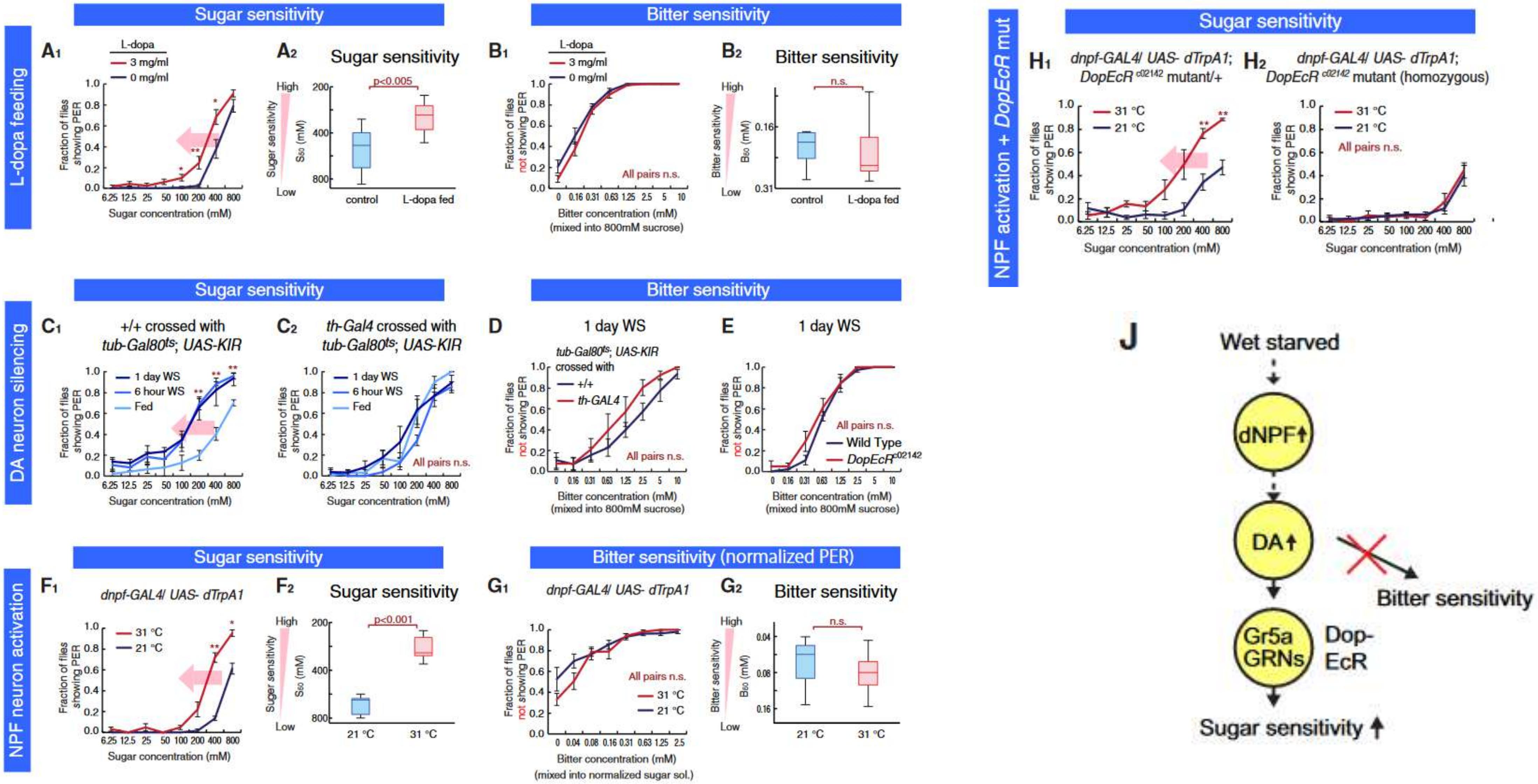


Starvation affects the taste sensitivity of fruit flies

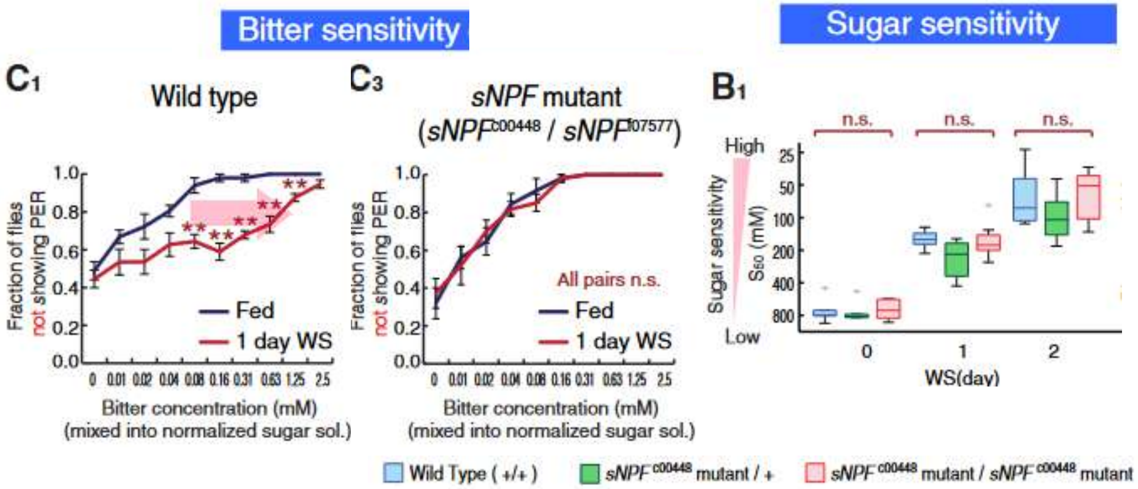


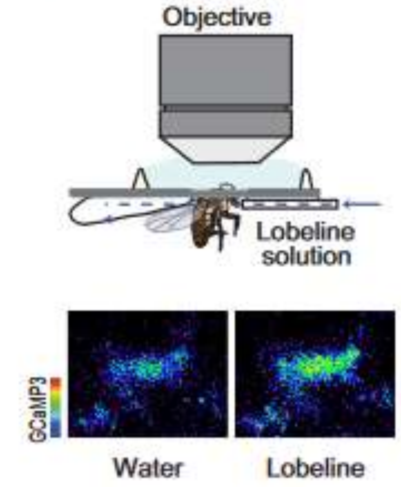


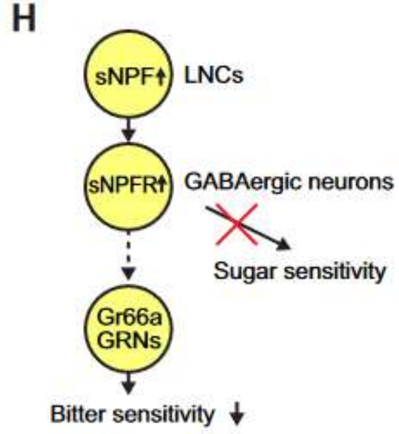
Neuronal pathway regulating sugar sensitivity during starvation

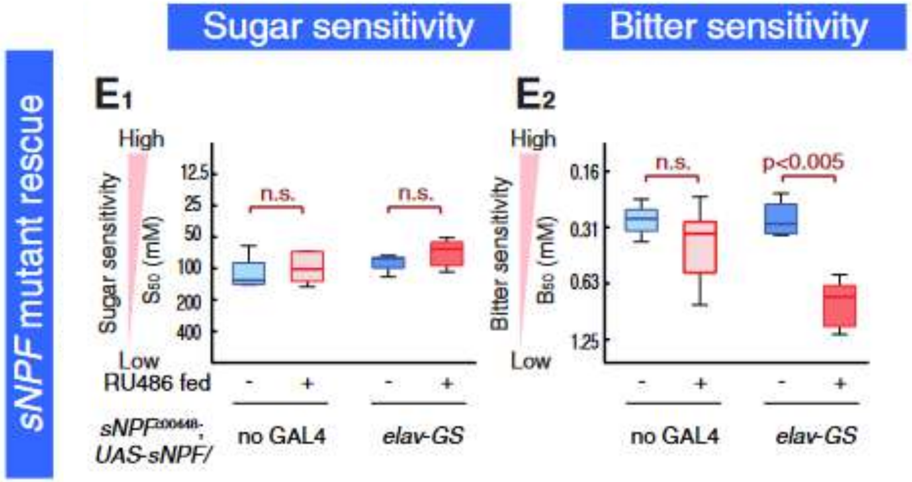


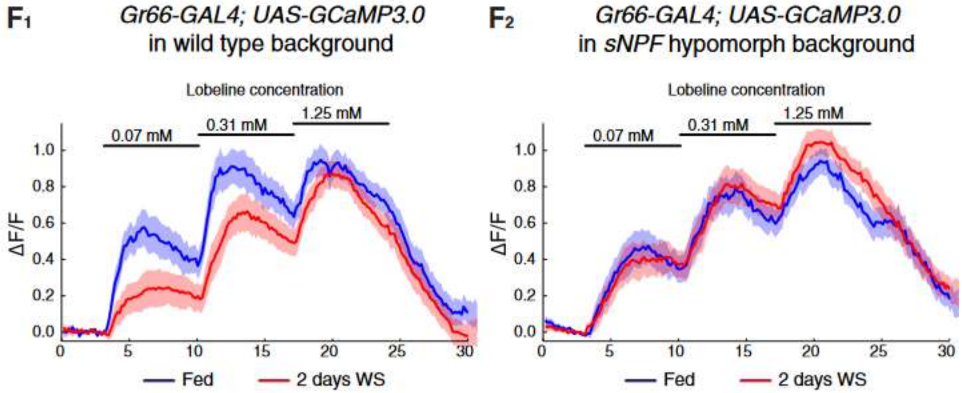
Subsets of sNPF neurons regulate bitter sensitivity during starvation



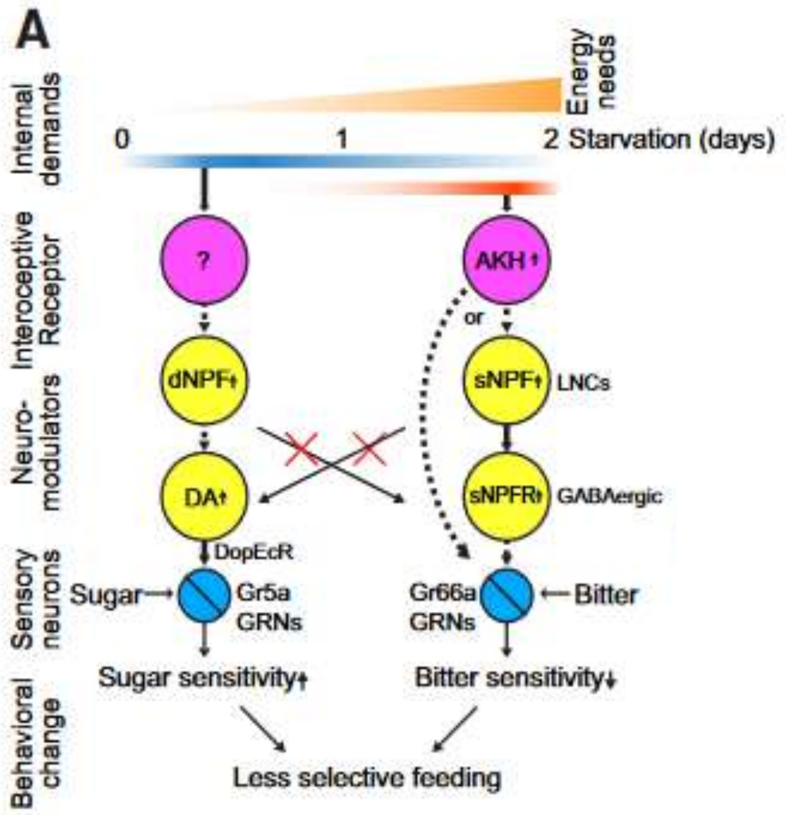








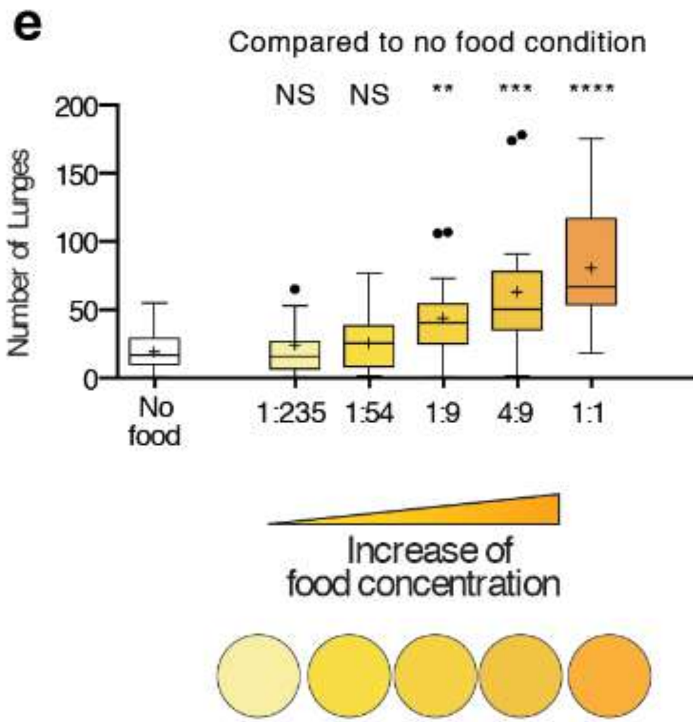
Distinct neuronal pathways modulating sugar and bitter sensitivity during starvation

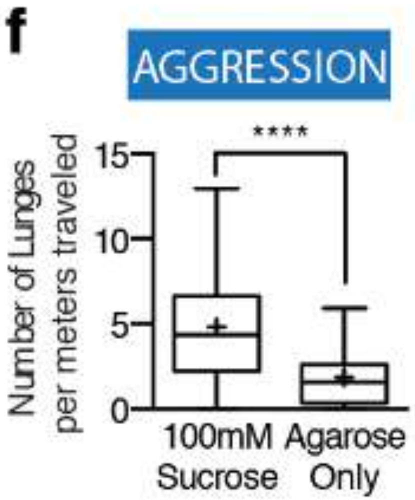


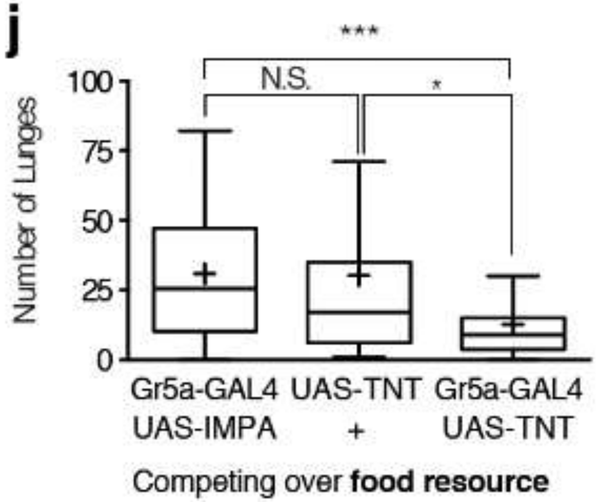
How Food Controls Aggression in *Drosophila*

Rod S. Lim[1,2], Eyrún Eyjólfsdóttir[3], Euncheol Shin[4], Pietro Perona[3], David J. Anderson[1,2]*

1 Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, California, United States of America, **2** Howard Hughes Medical Institut California Institute of Technology, Pasadena, California, United States of America, **3** Division of Engineering and Applied Sciences, California Institute of Technolog Pasadena, California, United States of America, **4** Division of Humanities and Social Sciences, California Institute of Technology, Pasadena, California, United States c America







Take home messages

- Bitterness and sweetness regulate aversion and attraction behavior independently
- Mechanical signals can interact with sweetness
- The mechanism of non-taste information integrate with sweetness is unclear.

Thanks!